Screening for Elevated Lead Levels in Childhood and Pregnancy

Update of 1996 USPSTF Review

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Appendix 1. U. S. Preventive Services Task Force Quality Rating Criteria

1996 Recommendations

B Recommendation

In 1996, the Task Force recommended screening for elevated lead levels at least once at age 12 months in all children with identifiable risk factors, and in all children living in communities in which the prevalence of blood lead levels requiring individual intervention, including residential lead hazard control or chelation therapy, was high or was undefined. There was insufficient evidence, however, to recommend a specific community prevalence below which targeted screening could be substituted for universal screening.

C Recommendation

The Task Force found insufficient evidence to recommend for or against routine screening for lead exposure in asymptomatic pregnant women.

C Recommendation

The Task Force also found insufficient evidence to recommend for or against trying to prevent lead exposure by counseling families to control lead dust by repeated household cleaning, or to optimize caloric, iron, and calcium intake specifically to reduce lead absorption.

Methods for Updating the 1996 Report[1]

Problem Formulation

Members of the USPSTF defined the scope of this update, in cooperation with the Agency for Healthcare Research and quality (AHRQ) and the Oregon Evidence Based Practice Center (EPC) personnel. The Task Force's goals for this update were to address the gaps in the literature revealed in the 1996 USPSTF recommendations.[2] These gaps related to the accuracy of risk assessment questionnaires in children with varying blood lead levels, the population prevalence at which to change from targeted screening to universal screening, the effectiveness of interventions to lower lead levels, and cost-effectiveness analyses of lead screening programs.

Search for New Studies

EPC personnel searched MEDLINE®, reference lists of review articles, and tables of contents of leading pediatric journals for studies published in1995 or later that contained new information about the prevalence, diagnosis, natural course, or treatment of elevated lead levels in asymptomatic children ages 1-5 and in pregnant women. Articles that met the following criteria were included in this update:

1) The study was an original meta-analysis, prospective cohort study, controlled trial, quasi-experimental study with concurrent controls, or case-control study; not a case series, case report, or comparison with historical controls.

2) The study was not included in the 1996 review.
3) The study was rated at least "fair-quality" using the USPSTF criteria (Appendix 1) for internal validity.

Synthesis

This report uses text and format from the 1996 report[1] on lead screening, updating the text and citations where appropriate. Members of the USPSTF and AHRQ identified critical issues for updating the 1996 USPSTF guidelines for lead screening. To prepare this update, we reviewed trials and epidemiologic studies published since January 1995 bearing on these critical issues. For the critical key questions only (below), we used standard USPSTF methods[3] to abstract information about the design, results, and internal validity of each study, and included only those studies we rated fair-quality or better. We reviewed the populations of asymptomatic children and pregnant women separately.

Key questions in the 2005 work assignment for CHILDREN were stated as follows:

- KQ1: Is there direct evidence that screening for lead results in improved health outcomes (i.e. cognitive changes, behavioral problems, learning disorders)?

- KQ2: What is the prevalence of elevated lead in children? Are there population-level risk factors that identify children at higher risk for elevated lead levels (i.e., geography, race/ethnicity, socioeconomic status, age)?

- KQ 3: Can screening tests accurately detect elevated blood lead levels? What is the accuracy of using questionnaires (or other tools) for risk factor assessment at various blood lead levels? What is the optimal frequency for screening? What is the optimal frequency for repeat testing?

- KQ4: What are the adverse effects of screening?

- KQ5: Do interventions (i.e. counseling families to reduce lead exposure, nutritional interventions, residential lead hazard control techniques, chelation therapy) for elevated lead levels result in improved health outcomes?

- KQ6: What are the adverse effects of interventions?

- KQ7: What are cost effectiveness issues?

Members of the USPSTF and AHRQ identified KQs 1 and 5 as critical key questions. We therefore updated KQs 1 and 5 using standard systematic review procedures. We conducted a selected review of the literature that addressed KQs 2-4, 6, and 7.

Key questions in the 2005 work assignment for PREGNANT WOMEN were stated as follows:

- KQ1: Is there direct evidence that screening in asymptomatic pregnant women for lead results in improved health outcomes (i.e., cognitive changes in offspring, perinatal outcomes including birth weight/preterm delivery etc, maternal blood pressure)?

- KQ2: What is the prevalence of elevated lead in asymptomatic pregnant women? Are there population-level risk factors that identify pregnant women at higher risk for elevated lead levels (i.e., geography, racial/ethnicity, socioeconomic status, age)?

- KQ3: Can screening tests accurately detect elevated blood lead levels? What is the accuracy of using questionnaires (or other tools) for risk factor assessment at various blood lead levels?

- KQ4: What are the adverse effects of screening?

- KQ5: Do interventions (i.e., counseling families to reduce lead exposure, nutritional interventions, residential lead hazard control techniques, chelation therapy) for elevated lead levels result in improved health outcomes?

- KQ6: What are the adverse effects of the interventions?

- KQ7: What are cost effectiveness issues?

We used standard systematic review procedures to address KQs 1 and 5. We conducted a selected review of the literature on pregnant women for KQs 2-4, 6, and 7.

New studies or information for key questions for children and pregnant women are discussed throughout the text below using the format from the 1996 chapter for this topic.

Results

Key Question 1: Screening in children and asymptomatic pregnant women

There is no direct evidence from controlled studies that screening children for elevated blood lead levels results in improved health outcomes. There is no direct evidence from controlled studies that screening improves maternal hypertension, cognitive changes in offspring or perinatal outcomes.

Key Question 2: Prevalence; Burden of Suffering

Summary: The prevalence of elevated blood lead levels among children and women in the United States, like that in the general population, continues to decline sharply, due primarily to marked reductions in lead in gasoline, air, dietary sources, and residential paint. However, the prevalence still varies substantially among different communities and populations, and children

and pregnant women share many of the same risk factors for elevated blood lead. Correlates of higher blood lead levels at all ages include minority race/ethnicity; urban residence; low income; low educational attainment; older (pre-1950) housing; home renovation or remodeling; pica; use of ethnic remedies, cosmetics, and lead glazed pottery; occupational and para-occupational exposures; and recent immigration. Alcohol use, smoking, pica, and immigration status have been demonstrated as risk factors among pregnant women.

Recent observational studies have demonstrated an inverse relationship between historical blood lead levels in children and subsequent measures of behavioral and cognitive performance at blood lead levels of <10 micro-g/dL. Recent observational studies provide limited, preliminary data that prenatal blood lead levels <10 micro-g/dL may be associated with neurodevelopmental delay or impairment. Study design and measurement issues, however, limit interpretation of these studies. Studies also suggest that levels of maternal exposure in this range may be associated with increased risk for spontaneous abortion, hypertension in pregnancy, and adverse effects on fetal growth[4].

What is the prevalence of elevated lead in children?

The prevalence of elevated blood lead levels in the U.S. population continues to decline sharply, due primarily to marked reductions in lead in gasoline, air, dietary sources, and residential paint.[5] In a 1999-2002 national survey of children aged 1-5 years, 1.6% had blood lead levels ≥10 micro-g/dL, compared to 9% in a similar survey in 1988-1991.[6] (The units micrograms/deciliter (micro-g/dL) will be used throughout this chapter: to convert to micro-mol/L, divide by 20.72.) Although the prevalence of elevated blood lead levels among children ages 1-5 years declined by 64% from 1991-94 through 1999-2002, the prevalence still varies substantially among different communities and populations, and an estimated 310,000 children remain at risk for exposure to harmful levels of lead.[5]

What is the prevalence of elevated lead in asymptomatic pregnant women?

Blood lead levels and blood umbilical cord lead levels are frequently used to assess both the mother's and fetus' levels of lead exposure and risk. In 1992, two large surveys of low-income pregnant women found 0%[7] and 6%[8] with blood lead levels >5 micro-g/d. A study of all women who enrolled in prenatal clinics in Mahoning County, Ohio, from 1990 to1992 found that 13% of prenatal patients had blood lead levels ≥10 micro-g/dL, with 1% having blood lead levels greater than 15 micro-g/dL.[9] Population mean blood lead levels in women of childbearing age and pregnant women have fallen over the past two decades. Although it was estimated in 1990 that 4.4 million women of childbearing age, and over 400,000 pregnant women, had blood lead levels of >10 micro-g/dl,[10] a recent study of 1109 infants in Quebec, Canada, found a mean cord blood lead of 1.5 micro-g/dL (0.076 umol/l; 95% CI = 0.074, 0.079).[11] In a recent review of NHANES data of 4,394 women of child-bearing age, the GM blood lead levels 1.78 micro-g/dL[12] and a longitudinal study of pregnant women in Boston demonstrated that umbilical cord blood lead levels declined 82% between 1980 and 1990.[13]

Are there population-level risk factors that identify children at higher risk for elevated lead levels (i.e., geography, race/ethnicity, socioeconomic status, age)?

The highest geometric mean blood lead levels (GM blood lead levels) in the U.S. occur in children aged 1-5 years (GM 1.9 micro-g/dL) and in adults ≥60 years of age (GM 2.2 micro-g/dL), with the lowest in youth aged 6-19 years (GM 1.1 micro-g/dL).[5] Children under 5 years of age are at greater risk for elevated blood lead levels and lead toxicity because of increased hand-to-mouth activity, increased lead absorption from the gastrointestinal tract, and the greater vulnerability of a developing central nervous system.[14] Geometric mean levels are significantly higher in males than in females except among children aged 1-5 years.[5]

Correlates of higher blood lead levels at all ages include minority race/ethnicity, urban residence, low income, low educational attainment, older (pre-1950) housing, and recent immigration.[5, 15-19] These factors are associated with increased exposure to important lead sources, including dilapidated housing with lead-based paint, lead-soldered pipes and household lead dust, and lead in dust and soil from heavy traffic and industry.[20-25] There have been major reductions in the number of U.S. homes with lead-based paint from the estimated 64 million in 1990, but approximately 24 million housing units still contain substantial lead hazards, with 1.2 million of these units occupied by low-income families with young children.[5, 26]

Other potential sources of household lead exposure include clothing or waste material brought home by workers in lead-using industries or hobbies, lead-based paint and dust contamination in pre-1978 housing undergoing remodeling or renovation, [19] dietary intake from lead-contaminated consumer products, drinking water, and lead-based pottery, and traditional ethnic remedies.[5, 27-30]

Geometric mean blood lead levels among African-American children (2.8 micro-g/dL) remain significantly higher than Mexican American children (1.9 micro-g/dL) and non-Hispanic whites (1.8 micro-g/dL). Even among low income families, however, GM blood lead levels declined significantly from 1991-1994 (3.7 micro-g/dL) to 1999-2002 (2.5 micro-g/dL).[5]

Are there population-level risk factors that identify pregnant women at higher risk for elevated lead levels?

A woman of childbearing age with a high blood lead level risks transmitting a high blood lead level to her unborn child.[31] Ethnic background, country of origin, and immigrant status of birth mothers, as well as lifestyle, age, and work patterns of pregnant women have shown to be associated with prenatal lead exposure in newborns. Multivariate analyses of pregnant women in Quebec, Canada, revealed that both cigarette smoking (15% increase) and alcohol intake (17% increase) make significant and independent contributions to cord blood lead concentrations.[32] In a survey of 10 Quebec hospitals, umbilical cord blood samples were obtained from 1,109 newborns. Although blood lead levels were considered low, a statistically significant relationship was observed between maternal age, and smoking during pregnancy, in cord blood lead concentrations.[11]

One hundred fifty-nine mother-infant pairs from a cohort of women receiving prenatal care in Pittsburgh, Pennsylvania, provided blood samples at delivery for lead determination. Alcohol use was associated with relatively greater cord blood lead compared with maternal blood lead. No association was found with cord blood lead or maternal blood lead with smoking, physical exertion, or calcium consumption.[33]

A recent study in New York City of pregnant women in their third trimester with an incident blood lead level (blood lead levels) of 20 micro-g/dL or greater showed they had newborns with a median incident blood lead level of 12 micro-g/dL. In addition, maternal blood lead levels were directly associated with gestational age and pica behavior. These cases were more than twice as likely to be foreign-born women.[34] Maternal immigrant status and pica behavior are also associated with high infant blood lead level.

Neurotoxic effects of lead exposure in children

Very high levels of inorganic lead exposure can produce serious neurological complications, which may result in death or long-term sequelae.[21, 35, 36] A number of adequately designed and conducted prospective cohort studies from a broad range of child populations have reported that a rise in blood lead from 10 to 20 micro-g/dL is associated with a likely decrement of 2-3 points (reported range -6 to +1) in intelligence test scores (IQ).[37-43] The variety of test instruments that have been used, and differences in adjustment for important covariates, make direct comparison of these studies difficult, but a consistent negative effect on intellectual development is reported.

In these studies, the mean blood lead levels at age 1-2 years (7.7-35.4 micro-g/dL) were higher than the current U.S. mean for this age group, but most levels were below 35 micro-g/dL. A meta-analysis[44] that included the five oldest of these cohort studies concluded that a doubling of blood lead levels from 10 to 20 micro-g/dL measured at age 2 years was associated with a statistically significant mean reduction of 1-2 IQ points; evidence was inconclusive regarding an association of IQ with mean postnatal blood lead levels. Significant associations have been demonstrated between umbilical blood lead levels and neurodevelopmental testing at 2 years of age, although the association was not significant at later ages. Blood lead levels at 2 years of age, however, were associated with neurocognitive performance at 10 years of age.[14] A recent analysis of school-aged children demonstrated a stronger cross-sectional inverse association of IQ with contemporary blood lead levels (mean BLL = 8 mcg/dL at age 7 years) than with baseline blood levels (mean BLL = 26 mcg/dL at 24 months old), suggesting an ongoing adverse effect of lead on cognitive performance among school-aged children.[45]

Although most cross-sectional studies evaluating the association of tooth and blood lead with IQ display methodological weaknesses such as selection bias and limited adjustment for covariates, they have been generally consistent in reporting small negative effects of elevated lead levels on IQ.[44, 46] A meta-analysis that included studies of whole tooth lead published since 1979 reported a statistically significant 1-point reduction in IQ associated with a doubling of tooth lead from 5 to 10 micro-g/g.[44]

Cross-sectional studies[47-51] have consistently reported small, inverse associations between blood or tooth lead and reaction (attentional) performance, but studies evaluating the effect of mildly elevated lead levels on other measures of neurodevelopmental function (e.g., behavior, learning disorders, auditory function) have produced inconclusive results. These have been less thoroughly evaluated than IQ, however, and more recent studies suggest associations between childhood lead exposure and disorders of attention and learning, and aggressive and delinquent behavior.[14, 35, 52, 53]

In most studies, the size of the estimates of lead effects on IQ are reduced when adjusted for potentially confounding variables,[44]suggesting that some of the observed association may be due to imperfectly measured or unmeasured covariates. Studies in rodents and primates, however, which can avoid most of the methodological weaknesses of observational studies in humans, report cognitive, attentional, and behavioral deficits, as well as auditory and visual dysfunction, with mildly elevated blood lead levels,[54-56] supporting a causal relationship between low-level lead exposure and neurotoxic effects in children.

A growing number of human epidemiology studies have reported associations between neurotoxic effects and blood lead levels once thought to be harmless. Several recent studies have demonstrated an inverse relationship between historical blood lead levels and subsequent measures of intellectual and cognitive performance at blood lead levels of <10 micro-g/dL. The shape of the dose-response curve at levels below 10 micro-g/dL is uncertain although data suggests that lead associated cognitive changes may be greater with incremental changes in blood lead levels in this range.[14, 35, 53, 57-60] A recent meta-analysis of seven prospective international cohort studies found evidence of deficits on standard IQ testing among children with maximal blood lead levels <7.5 mcg/dL. A decline of 6.2 IQ points (95% CI, 3.8-8.6) was observed as blood lead levels increased from 1 to 10 mcg/dL.[61]

Lead-associated effects on neurobehavioral functioning must be considered relative to other important covariates such as socioeconomic status, home and parenting environment, and genetic factors.[57] The contribution of childhood lead exposure to the observed variance in cognitive ability (IQ testing) is believed to be in the range of 1-4%, while social and caregiving factors may be responsible for 40% or more.[52, 57] Blood lead levels, however, represent a larger proportion of the known, modifiable variance in children's cognitive ability.

Adverse effects of lead exposure on pregnancy outcomes

The effects of very high blood lead levels during pregnancy on reproductive outcomes such as abortion and stillbirth have been recognized for many years.[21] Observational studies in pregnant women with blood lead levels <30 micro-g/dL have reported associations between elevated levels and birth weight, length of gestation (including preterm delivery), and neonatal head circumference.[62-69] The associations have been small, variable in direction of effect, and not statistically significant in most studies. These studies failed to detect important effects on other reproductive outcomes. Inconsistent results may be due in part to imprecise measures of fetal lead exposure.[68-72] All but one[42] of six previously cited cohort studies,[37-42] as well as the meta-analysis described above,[44] reported no association between antenatal or perinatal maternal blood lead levels and full-scale IQ measured at preschool or school age. Although very high lead levels in pregnancy are clearly hazardous, the adverse effects on the fetus of antepartum lead levels in the range typically found in the U.S. are not established.

Reproductive effects

A recent review summarizing the epidemiological literature on typical community lead exposure levels, other than those associated with high occupational hazards, states that prenatal lead exposure is unlikely to increase the risk of premature membrane rupture but does appear to

increase the risk of preterm delivery. This review goes on to stay that is it unclear whether prenatal lead exposure decreases infant gestational age and that increased exposure appears to be associated with reduced birth weight, but that results vary in relation to study design and degree of control for confounding. Adjustment for gestational age, a possible confounder of the birth weight-lead exposure association, did not yield clearer results.[73]

The Mexico City Prospective Lead Study examined the association of maternal prenatal blood lead level during pregnancy (range 7.5-9.0 micro-g/dl [0.36-0.43 –micro-mol/l]) and child postnatal blood lead level (range of median blood lead level from birth to 48 months 7.0-10.0 micro-g/dl [0.34-0.48 micro-mol/l]) with head circumference, in a sample of Latino immigrants living in Los Angeles. Multiple regression modeling showed significant negative associations ($p<0.05$, two-tailed) between 6-month head circumference and 36-week maternal blood lead level, and 36-month head circumference and 12-month blood lead level; however, these were the only significant associations among the over fifty assessed in this study.[74]

In 272 mother-infant pairs, tibia bone lead was the only lead biomarker clearly related to birth weight (other significant birth weight predictors included maternal nutritional status, parity, education, gestational age, and smoking during pregnancy). Findings suggest that bone lead might be a better biomarker of lead body burden than blood lead.[75]

Neurodevelopmental and cognitive measures and lead effects

Recent observational studies (prospective cohort and cross-sectional) provide limited, preliminary data that prenatal blood lead levels may be associated with neurodevelopmental delay or impairment. Study design and measurement issues, however, limit interpretation of these studies.

A prospective study of 103 African American neonates with low-level parental lead exposure included a battery of 16 neonatal behavioral assessments at 1 to 2 days after birth. No differences were found in 15 of the 16 domains studied, with neonates in the higher exposure group receiving lower scores on the hand-to-mouth motor activity than did those infants in the lower exposure group ($P< 0.05$).[76] A sample of 79 African-American infants with low-level prenatal parent lead exposure were given the Fagan Test of Infant Intelligence (FTII) battery at 7 months of age.[77] Excluding all but infants with scores in the 5th and 95th percentiles of the FTII (n=5 in both groups) revealed that subjects rated at high risk for impairment on the FTII (those in the loweest 5th percentile) were 6 times more likely to be in the highest maternal blood lead level quartile ($P< .004$). Infants scoring in the lower 15th percentile (n=12), were 2 times more likely to be in the high maternal blood lead level quartile, though significance dropped to $P<0.056$.[77] The difference between the mean blood lead levels in the infants with lowest and highest FTII scores (5th and 95th percentiles) was very small, however (0.44 vs. 0.94 mcg/dL). Recent evidence suggests that children may demonstrate differences in evoked visual and auditory potentials associated with increased levels of prenatal lead exposure.[78, 79]

Other adverse effects of lead exposure

Lead exposure affects many organ systems, including cardiovascular, renal, and hepatic, but most clinically apparent (i.e., symptomatic) effects occur with blood lead levels ≥50 micro-g/dL.[21, 80-83] Subclinical effects on renal function can be observed at lower levels of exposure and children may be more vulnerable.[84, 85] Small increases in systolic blood pressure have been associated with mildly elevated blood lead levels (i.e., 1-3 mm Hg for a rise in blood lead from 10 to 20 micro-g/dL) in most large, population-based, cross-sectional studies evaluating nonpregnant adults and pregnant women.[86-92] In children, evidence of blood pressure effects is more limited: one cross sectional study found no association between elevated blood lead levels (range 7-70 micro-g/dL) and elevated blood pressure.[93] Adverse effects on height from lead levels well below 40 micro-g/dL have been suggested by analyses of national cross-sectional data,[94, 95] but cohort studies with more extensive covariate adjustment report either transient or no effect of elevated lead levels (peak sample means 11-17 micro-g/dL) on growth.[43, 96, 97]

In a cohort of women in their third trimester, immigrant women were more likely to have elevated blood lead levels and elevated blood pressure, compared to non-immigrant women. An association between elevated blood level and blood pressure was significant only in the immigrant group.[98] Past lead exposure was associated with hypertension and elevated blood pressure during pregnancy. Bone lead concentration, however, was not shown to be related to hypertension or elevated blood lead in pregnancy.[99]

Among 110 women in their third trimester, gestational hypertension cases showed significantly higher blood lead levels than normotensives, and blood lead was significantly related to blood pressure, even after correcting for body mass indices and age. The lead:ionized calcium ratio showed a stronger association with blood pressure than lead alone.[100] A cross-sectional study of 39 pregnant women in the third trimester of pregnancy compared red blood cell (RBC) levels of lead (Pb) and blood pressure. The study population included 20 women with normal pregnancies, 15 with mild hypertension, and 4 with severe hypertension and preeclampsia. Preeclamptic pregnancies were more likely to have an elevated RBC Pb. Rank correlation showed a significant effect of RBC Pb level on blood pressure.[101]

Key Question 3: Accuracy of Screening Tests

Can screening tests accurately detect elevated blood lead levels?

Screening tests considered for detecting lead exposure include blood lead and free erythrocyte (or zinc) protoporphyrin levels. Blood lead concentration is the more sensitive of the two for detecting modest lead exposure, but its accuracy, precision and reliability can be affected by environmental lead contamination during blood collection, day-to-day biologic variability, and laboratory analytic variation. Lead contamination of collecting equipment and skin contamination during capillary sampling may each positively bias blood lead levels by up to 1.0 micro-g/dL, on average, although individual effects of skin contamination may be much greater.[102-106] Studies defining abnormal results as blood lead levels above 10 or 20 micro-g/dL have reported false-positive rates of 3-9% for capillary sampling, compared to simultaneously collected venous blood lead.[103, 104] Day-to-day biologic variability and trends over time contribute to higher false-positive rates for initial capillary samples when compared to results

from venous testing done at a later date.[103, 107] False-negative rates with capillary sampling appear to be lower, reported in one study as 1-8% compared to venous blood.[104] In published surveys,[102, 108] about 80-90% of clinical laboratories participating in proficiency testing programs met performance criteria for blood lead (within +/-4 micro-g/dL of target values, for values <40 micro-g/dL,[108] unpublished national data show >95% of participating laboratories meeting these criteria and >80% achieving accuracy to within +/-2 micro-g/dL of target values (unpublished data, Centers for Disease Control and Prevention, November 1993). Nonparticipating laboratories are likely to be less proficient. Reported blood lead values may differ by as much as 5 micro-g/dL from true values due to these sources of variability and bias, and these divergences may affect the predictive value of a positive test. Results from capillary samples may vary even more, although recent studies suggest that the positive bias can be reduced with increased attention to reducing skin lead contamination.[103, 104]

The erythrocyte protoporphyrin (EP) test, an indirect measure of lead exposure based on lead's effects on the hematopoietic system, is unaffected by contamination with environmental lead and is easily performed on capillary blood specimens, making it more acceptable for use with young patients. Erythrocyte (or zinc) protoporphyrin is insensitive, however, to modest elevations in blood lead levels.[8, 109-115] The test also lacks specificity,[8, 109, 110, 112, 113, 116] thus limiting its predictive value. In one study, EP measurements were taken on 47,230 suburban and rural children, and although 4.7% of the children had an elevated erythrocyte protoporphyrin level, only 0.6% had elevated blood lead levels.[117]

What is the accuracy of using questionnaires (or other tools) for risk factor assessment at various blood lead levels?

In communities where there is a low prevalence of lead levels requiring individual intervention with chelation or residential lead hazard control, blood lead screening will have a low yield with many unaffected children undergoing testing at potentially high cost and inconvenience. Cross-sectional studies[118-123] in urban and suburban, mostly Midwestern, populations have shown that one or more positive responses to five questions (about exposures to deteriorated paint from older or renovated housing, to other lead-poisoned children, or to lead-related hobbies or industry)[124] detects 64-87% of children with blood lead levels >=10 micro-g/dL. Three studies reported higher sensitivities (81-100%) for blood lead levels >=15-20 micro-g/dL.[120, 121, 123] None of these studies evaluated the ability of questionnaires to detect levels above 20 micro-g/dL, in part because so few patients had levels so high. Specificity among the studies ranged from 32% to 75%. In the samples with a lower prevalence (2-7%) of levels >=10 micro-g/dL, the proportion of individuals with a negative questionnaire who had elevated blood lead levels was predictably low (0.2-3.5%), but increased to 19% when the population prevalence of elevated lead levels was higher (17-28%).

More recent studies of the utility of questionnaires to assess the risk of lead exposure in children in both urban and rural settings have demonstrated a low prevalence of elevated blood lead levels and poor sensitivity and specificity.[125-128] Studies of questionnaires modified for local use provide some evidence of clinical utility for identifying children with elevated blood lead levels,[128, 129] compared to the standard CDC questionnaire.

Other studies have reported high false-positive rates for questionnaires[126, 128] and that resource considerations[125] are important when formulating a screening program. A population-based follow-up study (n=31904) showed that raising the action level for screening to 15 micro-g/dL in this sample would have eliminated the unnecessary follow-up of 5,162 children, 3,360 of whom were falsely identified as having elevated lead levels.[130]

A recent study identified housing risk factors associated with elevated blood lead levels (≥10 mcg/dL) among 481 children residing in Rochester, New York. Housing characteristics including rental status, lead-contaminated floor dust, and poor housing condition were all associated with EBLL (sensitivity 47-92%, specificity 28-76%, positive predictive value 25-34%, negative predictive value 85-93%), suggesting that housing characteristics and floor dust lead levels can be used to identify homes where a lead hazard may exist before or during occupancy.[131]

Prenatal screening with questionnaires

A maternal survey using four questions recommended by the CDC was evaluated in a study of 314 new prenatal patients. In this sample, the prevalence of elevated maternal lead levels (at or greater than 10 micrograms/dL or 0.483 mumol/L) was 13%. Subjects with a positive response to at least one question were more likely to have elevated blood lead than those who answered negatively to all four questions (relative risk = 2.39, 95% confidence interval 1.17-4.89; P = .01). The CDC questionnaire had a sensitivity of 75.7%. Among women who answered "no" to all 4 questions, the probability of having an elevated lead level was reduced from 13% to 6.9% (negative predictive value of 93.1%). The most predictive single item was 'home built before 1960.' The study also identified a high prevalence of elevated blood lead among children living with women with elevated blood lead levels.[9]

Key Questions 5: Effectiveness of Early Detection

Detection of lead exposure before the development of potentially irreversible complications permits the clinician to recommend environmental interventions to limit further exposure and, when necessary, to begin medical treatment with chelating agents. Early detection may also result in interventions that prevent exposure of other children to lead (the child with elevated blood lead level acting as a sentinel for a hazardous environment). There is relatively little convincing evidence that these interventions improve health, however. One issue is that most available studies in asymptomatic children evaluate the effects of various interventions on blood lead levels rather than on clinical outcomes. Second, blood lead levels in childhood, after peaking at about 2 years of age, decrease even without intervention.[6] Longitudinal studies of asymptomatic children with elevated lead levels show reductions in blood lead levels during short- and long-term follow-up in the absence of any intervention,[132, 133] a result attributable at least in part to regression to the mean, random variation, laboratory error, and redistribution from blood to other tissues. To evaluate adequately the effects of interventions on blood lead levels, studies must take into account these changes over time, preferably by the use of controls, individuals who do not receive the intervention.

Effect of screening on clinical outcomes

Evidence is not available to demonstrate that universal screening for blood lead results in better clinical outcomes than either screening targeted to high-risk persons or individualized testing in response to clinical suspicion. Several older studies reported that, compared to historical results from individualized testing, intensive screening programs targeted to children in high-risk neighborhoods reduced case fatality rates, mortality rates, and proportions of children detected with very high blood lead levels or who developed symptomatic lead poisoning.[134-136] In the absence of concurrent controls, it is not clear whether the reported reductions in mortality and case fatality rates were due to screening or to improvements in medical care over time. Reductions in mean lead levels may also have been due to secular trends, changes in screening tests, and to screening greater numbers of children, including many at low risk for severe lead poisoning. Thus, the available evidence regarding the efficacy of screening programs is weak.

Do interventions for elevated lead levels result in improved health outcomes?

There is substantial evidence that chelating agents benefit children with symptomatic lead poisoning, but no studies have demonstrated clinical benefits of chelation therapy in asymptomatic children. A large multicenter randomized controlled trial sponsored by the U.S. National Institute for Environmental Health Science (NIEHS) enrolled children in 1994-1997 to assess the effect of oral chelation therapy with succimer on IQ in young children with venous blood lead concentrations of 20-45 micro-g/dL.[137] Follow-up testing at 36 months demonstrated a mean IQ one point lower and a lower parental rating of behavior among the succimer group compared to placebo. Although succimer-treated children did slightly better on a test of learning ability, none of the differences between the groups were statistically significant.[138] Reanalysis of the same data using the change in blood lead level as the independent variable demonstrated a 4.0 point improvement in cognitive scores for every 10 micro-g/dL reduction in blood lead level, but only in the placebo group, suggesting that factors other than declining blood lead contributed to cognitive improvement, or that treatment had an adverse effect on cognitive performance.[139] Assessment of neurobehavioral outcomes at 7 years of age revealed no statistically significant differences on a battery of neurobehavioral tests, except that the succimer group had worse attention-executive function scores.[140] Treatment also appeared to have an adverse effect on mean height.[141] The Trial Group concluded that chelation therapy was not indicated for children with blood lead levels <45 micro-g/dL.[138, 140]

An observational study[142, 143] compared children with blood lead levels between 13 and 46 micro-g/dL (median 30 micro-g/dL), who did and did not receive EDTA chelation therapy depending on the results of a lead mobilization test. There was no effect of chelation on IQ at either 7 weeks or 6 months follow-up after controlling for age and initial IQ. Changes in concentrations of blood lead, bone lead, and EP also did not differ significantly between chelated and unchelated children. The greatest reductions in blood lead were associated with the highest initial lead levels, independent of chelation. The method of treatment assignment (i.e., based on a positive mobilization test) was most likely to have biased the study toward finding an effect of chelation, yet no effect was observed. Despite evidence of efficacy in lowering blood lead on a short term basis, there is little evidence presently available to confirm a clinical benefit from chelation

therapy for children with lead levels <45 micro-g/dL. Ethical considerations preclude such trials for children with blood lead levels above 45 micro-g/dL.

We found no studies evaluating clinical outcomes after residential lead hazard control.

Effects of chelation therapy on blood lead levels

In the previously cited NIEHS-sponsored RCT of oral chelation in young children with venous blood lead concentrations of 20-45 micro-g/dL (TLC Study), which reported no effects of chelation on IQ (Table 1),[137-140, 144] blood lead levels fell steeply in the treatment group in the first week (mean 11 micro-g/dL lower) but then began to rebound. Blood lead levels also dropped in the placebo group, but more slowly. Blood lead levels were 77% of baseline in the succimer group (88% of baseline among placebo) at seven weeks after initiation of therapy. Mean blood lead levels among the treatment group were 4.5 micro-g/dL and 2.7 micro-g/dL, at six and twelve months respectively, but by 24 months the difference between treatment and placebo groups was not significant.[144]

Chelating agents have demonstrated short-term reductions in blood lead levels in children whose pretreatment values ranged from 20 to 70 micro-g/dL in randomized comparative trials, case series studies, and uncontrolled experiments where chelation therapy was often combined with environmental interventions, but these reductions were not sustained over longer periods in the absence of repeated or continuing chelation therapy or environmental interventions.[145-152]

In other descriptive studies (case series, uncontrolled trials, etc.) of asymptomatic children with initial blood lead levels ranging from 40 to 471 micro-g/dL, chelating agents reduced blood lead levels substantially, to levels <40-70 micro-g/dL (varying with initial levels) and these reductions were maintained for weeks to years after therapy was discontinued (Table 1).[145, 153-157] Most of these children were also returned to homes that had undergone lead hazard reduction, however, and the effect of this additional intervention was not specifically evaluated.

These data provide good evidence that chelating agents may result in short-term reductions in blood lead levels in children but suggest that these reductions may not be sustained over longer periods in the absence of repeated or continuing chelation therapy or environmental interventions.

Effect of residential lead hazard control on blood lead levels

Summary: Recent studies of household dust and paint hazard control through cleaning, abatement and education have mixed results. Of the eight controlled studies published since 1995, one has shown a modest but significant decline, five have shown non-significant declines, and two have shown non-significant elevations in blood lead levels among children. Reduced blood lead levels were seen among children with higher baseline lead levels (15+ or 20+ micro-g/dL) in 2 studies (1 meta-analysis, 1 retrospective chart review with no comparison group), but not in children with lower baseline levels. Recent studies differ from older studies in that newer paint hazard control techniques result in lower dust lead levels. Population venous lead-levels

have decreased over time, and lead-poisoned children in older studies had higher mean Blood lead levels than in recent studies.

Detailed assessment: (Tables 2 and 3) For most asymptomatic children with elevated lead levels, the primary goal of intervention is to reduce exposure to lead-contaminated paint, dust, and soil in the child's home environment, since these sources account for most excess lead exposure. Newer residential lead-based paint hazard control methods can effectively reduce environmental exposure to lead paint and lead-contaminated dust[23, 158, 159] in contrast to older strategies that often increased lead exposure during the intervention. These newer techniques, however, can result in an elevation of blood lead in a subset of children immediately following lead control interventions. In an evaluation of HUD-sponsored lead control interventions among fourteen state and local governments, 81 of 869 children (9.3%) had an elevation of >= 5 micro-g/dL. Risk factors associated with post-intervention increases were the number of exterior paint deteriorations, the educational level of the female parent or caregiver and the younger age of the child.[160]

Pre-1996 retrospective cohort studies, case series, and uncontrolled experiments suggest that there is a modest decline (4-10 micro-g/dL) in mean blood lead levels in children with initial blood lead levels ≥ 25 micro-g/dL. More recent studies of newer lead-based paint hazard control techniques that included an untreated comparison group found small beneficial effects[161, 162] or no effects of intervention.[163, 164]

A meta-analysis of 4 randomized controlled trials conducted between 1996 and 2000, found that interventions had no effect on mean blood levels (-0.62 micro-g/dL, 95% CI -1.55 to 0.32), but that there were significant reductions in the proportion of children who had blood lead concentrations exceeding 15 micro-g/dL (6% vs. 14%, p=0.008) and 20 micro-g/dL (2% vs. 6%, p=0.024) in the intervention group compared with the controls.[165]

Two of these 4 trials evaluated dust control and two evaluated the provision of education and equipment to families. The earlier of the two trials of dust control (1998) evaluated one-time professional dust control and window sill paint sealing in homes of children aged 4 or younger, with mean blood lead of 16.9 micro-g/dL.[163] There were similar reductions in blood levels in the intervention and control groups (-6.2 vs. -5.9 micro-g/dL) 6 months after abatement. In the 2nd randomized trial (1999), conducted in Jersey City, New Jersey, investigators recruited children aged 6 to 36 months who had lead paint in the home. Families (n=113) were randomized to a lead exposure reduction group or to an accident prevention control group. In the lead exposure reduction group, staff members visited the home every two weeks and spent about 2 hours cleaning up dust. After 1 year, there was a small but statistically significant difference in blood lead change between intervention and control groups, adjusted for baseline lead levels (-2.1 vs. +0.1 micro-g/dL, p<0.05).[161] A subanalysis of this trial found that among 39 homes that received the intervention, only children in uncarpeted homes experienced a significant reduction in blood lead levels. Mean blood lead level decreased by 2.76 micro-g/dL (p=0.004) among children in uncarpeted homes, compared with a reduction of 0.84 micro-g/dL (p=ns) among children in carpeted homes.[166]

A follow-up study in urban children in a trial of chelation therapy vs. placebo examined the effects of a second professional lead dust cleaning of homes 18 months after an initial cleaning and commencement of therapy.[167] All homes in the Philadelphia site (n=165) of the TLC trial[144] were offered a second professional cleaning, and subject participation in the follow-up intervention was voluntary rather than randomized. The mean BLL at study initiation was 26 ug/dL, and the randomized trial found no difference in blood lead levels between the chelation and placebo groups. The mean BLL was 15.7 micro-g/dL at the second cleaning visit, and 6 months later there was no difference in blood lead levels between children whose homes were cleaned (n=73) and those whose homes were not cleaned (n=86). The report of the follow-up cleaning trial did not stratify results by the original treatment assignment of the subjects, so the effects of the combined interventions cannot be compared with an untreated group.

A 2003 retrospective cohort study identified children listed in the New York City child blood lead registry and compared blood levels before and 10-14 months after remediation with those of a control group that did not have remediation.[164] Mean blood levels declined significantly from 24.3 micro-g/dL to 12.3 micro-g/dL at follow up, regardless of remediation. After adjusting for confounders, the remediation effect was 11% (p=ns). Race was identified as the only confounding factor, and white and Asian children had an adjusted mean follow-up blood lead level 30% lower than African American children ($p<0.01$). The effect of remediation appeared to be stronger in younger children (10 -<36 months) than in older children (36-72 months.) Another retrospective cohort study that evaluated in-home counseling, combined with professional lead paint remediation, compared lead levels in children aged 6 months to 6 years with mean blood lead of 28.8 micro-g/dL with similar children who did not receive the intervention.[162] Follow-up blood lead was measured on average 69 days after abatement, 172 days after the initial sample. After adjusting for season and age of the child, the treatment group blood lead decreased 6.0 micro-g/dL from 28.8 to 22.8, and the effect of treatment was significant ($p<0.05$). The comparison group mean blood lead decreased 1.6 micro-g/dL from 31.1 to 29.5 (p=ns).

In a retrospective study that measured blood lead levels in children whose homes were abated between 1987 and 1990, before and after abatement policies in Massachusetts became more stringent in 1988, the mean blood lead decreased from 26.0 micro-g/dL at baseline to 21.2 micro-g/dL ($p<0.001$) measured between 2 weeks to 6 months post abatement. Reductions were only seen, however, among children whose baseline blood lead levels were greater than 20 micro-g/dL. This study found no meaningful change in pre to post abatement levels by calendar year of intervention.[168] The effect of different housing policies on the risk of subsequent lead exposure in homes where a child with elevated blood lead had resided in the past was demonstrated in adjacent geographic regions of two northeastern states. Approximately eight years later, the risk of identifying at least one child with an elevated blood lead level (≥10 mcg/dL) was four times greater in the state with less stringent housing-based lead poisoning prevention policies.[169]

A study of 1212 HUD dwellings that received interior treatment for lead hazard control in thirteen states from 1994 to 1998 reported a mean 2.8 micro-g/dL reduction in children's (n=240) blood lead levels at 12 months postintervention, from a median level of 10 micro-g/dL at baseline.[170] The effect of treatment in these studies was not compared with an untreated population. Another study of HUD dwellings in four Massachusetts communities found a

significantly larger decline in blood lead levels between 1993 and 2002 among children in treated homes than in untreated homes, matching on preintervention BLL. Children's BLLs decreased from 7.07 and 6.62 micro-g/dL to 3.59 and 4.28 in the treated and untreated homes respectively (p=0.015). The study adjusted for time and seasonality to account for the downward trend in BLLs observed among children in the general Massachusetts population, from 5.9 ug/dL in 1994 to 3.2 ug/dL in 2002.[171]

These trials also highlight important problems with using lead-paint hazard control as the sole method to reduce lead exposure. Poor inner-city families tend to move frequently, so that treating the current residence may have limited long-term benefit to the child, although benefit may accrue to other children moving into that residence. In the Jersey City study, for example, approximately 30% of the randomized families moved during the 12-month follow-up period.[161] Residential lead-paint hazard control is costly and labor-intensive, resulting in low rates of intervention, especially in poor communities.[22, 172] Lead dust is ubiquitous and highly mobile, so that recontamination by nearby lead sources, including soil lead, may occur after lead-paint hazard control efforts take place in a dwelling.[158, 173-175] These problems indicate a need for additional individual interventions, as well as more comprehensive community-based interventions, to reduce household lead exposure. Unfortunately, available data about programs that employ multiple interventions are sparse.[157, 160]

The small effect noted in studies evaluating lead-paint hazard control methods may be attributable in part to recontamination of the dwelling by nearby lead sources and from subsequent deterioration of painted surfaces.[158, 173, 174] Several studies have evaluated measures designed to reduce ongoing lead-dust contamination from lead-contaminated paint and soil. In a nonrandomized controlled trial among children with blood lead levels of 30-49 micro-g/dL, having a research team wet-mop all lead-contaminated interior surfaces twice a month with a high-phosphate detergent cleanser resulted in significantly greater adjusted declines in mean blood lead levels of children in intervention households compared to children in control households (6.9 vs. 0.7 micro-g/dL) at 1-year follow-up.[176]

Counseling and education interventions

Summary: Overall, there is insufficient evidence to determine whether education and counseling improves outcomes among children with moderately elevated blood lead levels. Blood lead reductions of varying magnitude occurred in children whose families received no intervention.

Detailed assessment: There have been no controlled studies to evaluate whether counseling families to perform cleaning would be as effective in reducing blood lead levels as professional cleaning. Two randomized controlled trials that administered counseling alone,[177] or with the provision of cleaning supplies,[178] found no significant effects of the intervention on children's blood lead levels. A retrospective cohort study of children with blood lead of 20-24 micro-g/dL found that a one-time in-home educational visit was associated with a greater reduction in blood lead after 6 months, compared with households that did not receive an educational visit (-4.2 micro-g/dL vs. -1.2 micro-g/dL, $p<0.001$).[179] In one uncontrolled experiment, the families of 78 children with blood lead levels of 10-35 micro-g/dL, who were living in the vicinity of a defunct

lead smelter, received intensive (30-45 minutes) in-home education and literature on prevention of lead exposure.[180] The mean blood lead levels in the 51 (65%) children who had follow-up blood lead levels at 4 months declined from 15.0 to 7.8 micro-g/dL (and maximum levels from 35.0 to 12.7 micro-g/dL). Without concurrent controls, it is not possible to determine how much regression to the mean and seasonal and age variations contributed to these reductions in blood lead levels. There is also evidence that clinician counseling at the worksite to reduce lead dust ingestion by workers (e.g., through personal hygiene practices) can significantly reduce mean blood lead levels at 1-year follow-up,[181] but this study also lacked controls and may not be generalizable to the residential setting.

Soil abatement

Summary: Recent studies of soil remediation in residential areas have shown only modest or non-significant effects.[175, 182, 183] Soil remediation in communities near lead mining, milling, or smelting operations may have a beneficial effect but was not considered within the scope of review.

A third focus of residential lead hazard control is exposure to soil lead. In a randomized controlled trial[173] of young children with initial blood lead levels of 7-24 micro-g/dL, extensive soil abatement, one-time dust abatement, and removal of loose interior paint resulted in a statistically significant reduction in mean blood lead levels of 1.2-1.3 micro-g/dL compared to loose paint removal alone. This clinically insignificant decline was associated with a substantial reduction in soil lead from a median 2,000 to 105 ppm. Preliminary results of the U.S. Environmental Protection Agency's Three City Urban Soil Lead Abatement Demonstration Project similarly suggest that substantial declines in soil lead cause only modest or no reduction in mildly elevated blood lead concentrations.[174, 175, 182, 183] The small effect was due at least in part to rapid recontamination with dust lead in households undergoing soil abatement. Among children living near a closed lead smelter, only 3% of the variance in blood lead levels was attributable to soil lead.[180]

An important potential public health benefit of residential lead hazard control is its effect on the lead levels or clinical outcomes of other children who live in the same household as a child identified with elevated lead levels, or who subsequently move into the remediated residence. Based on the biokinetics of lead,[21] it is reasonable to believe that environmental interventions conducted before children are exposed are likely to prevent increases in blood lead levels more effectively than the same interventions in children who have already been exposed. Cross-sectional surveys before and after soil abatement in the vicinity of a former smelting and milling operation observed a statistically significant reduction in blood lead levels among children aged 6-36 months who had not been exposed to lead-contaminated yards in early childhood. A significant reduction was not seen in children aged 36-72 months.[184]

Effect of nutritional interventions on blood lead levels

Summary: There is insufficient evidence to determine whether nutritional interventions are an efficacious route to lowering children’s blood lead levels.

Detailed assessment: In most settings, neither residential lead-based paint nor dust hazard control nor chelation therapy is routinely offered to children with blood lead levels <20 micro-g/dL, but some experts have recommended offering these children dietary counseling to reduce their blood lead levels.[124] There is limited, preliminary, and somewhat contradictory evidence that correcting such nutritional inadequacies will reduce blood lead levels or prevent further increases in children, depending on the nutritional intervention under investigation (Tables 4 and 5).[157, 185-194]

Three RCTs[185, 189, 190] and three prospective cohort studies[191, 192, 195] did not find a significant correlation between calcium and blood lead levels, although one prospective cohort study [196] found an inverse association. Fat and caloric intakes were positively associated with blood levels in a prospective cohort study[186] and a cross-sectional study.[188] Carbohydrates had an inverse association according to a prospective cohort study.[186] Two prospective cohort studies[191, 192] found that ferritin is not significantly related to blood lead levels. One cross-sectional study[12] found a positive association with folate and a negative association with serum folate. Iron has not been shown to have a effect on blood lead levels in two RCTs[185, 190] and one prospective cohort study,[157] although three prospective cohort studies[191, 192, 195] and one cross-sectional study[187] reveal a negative association, while one cross-sectional study shows a positive association.[12] Two RCTs[185, 190] found no correlation between blood lead levels and phosphorus. One cross-sectional study found a positive association between blood lead levels and pyridoxine.[12] Protein had a paradoxical effect in one prospective cohort study, significantly associating with low lead levels at 6 months, but then higher lead levels at 12 months.[191] Two prospective cohort studies showed no relationship between supplement use and blood lead levels.[191, 192] One cross-sectional study found a negative association between blood lead levels and thiamine.[12] Vitamin C is inversely related with blood lead levels according to a prospective cohort study.[186] Vitamin C has also been inversely associated with blood lead levels in a cross-sectional study,[193] Dietary vitamin D is also inversely related to blood lead levels according to a prospective cohort study,[192] whereas serum vitamin D has not been correlated with blood lead levels in two prospective cohort studies.[191, 192] Two prospective cohort studies yielded different results concerning zinc, showing no association to blood lead levels,[191] and conflicting results.[192]

Despite the significant relationships between nutrients and children's blood lead levels in the epidemiological studies described above, it is noticeable that none of the RCTs found significant correlations.[185, 189, 190] Similarly, a 2004 retrospective cohort study, using data from the Wisconsin Childhood Lead Poisoning Prevention Program in children aged 0-6, compared blood levels of children enrolled in the Special Supplemental Nutrition Program for Women, Infants, and Children from 1996 to 2000 with blood levels of children not enrolled in the nutrition program, and did not find any significant differences between the two groups.[194] Other cohort studies reveal significant association with calories, carbohydrates, fat, iron, vitamin C and vitamin D,[157, 186, 191, 192, 195, 196] whereas the cross-sectional studies demonstrate significant associations with ascorbic acid, calories, fat, folate, serum folate, iron, pyridoxine, and thiamine.[12, 187, 188, 193] Adverse effects were reported in two of the fourteen studies; both are RCTs. A calcium study using a 1800 mg/d[189] dosage reported abdominal pain in both the treatment and control groups. A calcium glycerophosphate-supplemented infant formula study reported elevated ratios of urinary calcium to creatinine and low concentrations of serum ferritin,

but these effects also occurred in both the treatment and placebo groups.[190] None of the other studies reported adverse effects.

A recent review concluded that experimental studies in animals and observational studies of humans provide evidence that calcium supplementation during the second half of pregnancy may reduce prenatal lead exposure by reducing mobilization of lead from bone.[197]

Key Questions 4 and 6: Adverse Effects of Screening and Intervention

The most common adverse effects of screening for elevated lead levels are false-positive fingerstick results, and the anxiety, inconvenience, work or school absenteeism, and financial costs associated with return visits and repeat tests. An EDTA lead mobilization test, used for some children with blood lead levels of 30-44 micro-g/dL,[198] requires intramuscular or intravenous infusion, a stay at the clinical center for at least 8 hours, and for young children, application of urine collection bags.[199] Residential lead-based paint and dust hazard control, when improperly done,[23] may produce acute increases in blood lead levels in resident children and abatement workers, occasionally necessitating hospitalization and chelation therapy.[200-204]Currently recommended techniques for lead hazard reduction are likely to reduce these adverse effects.[23] Chelating agents for asymptomatic lead poisoning have also been associated with important adverse effects. EDTA and dimercaprol (BAL) have transient renal, hepatic, and other toxicity, require intravenous or intramuscular injection, and generally require hospitalization for administration.[124, 205, 206] Common adverse effects of d-penicillamine are penicillin-like sensitivity reactions and transient nephrotoxicity which may be dose-related [207]; there are rare life-threatening reactions.[124, 134, 147, 156] Adverse effects of succimer (meso-2,3-dimercaptosuccinic acid, or DMSA) include mild gastrointestinal (vomiting and diarrhea) and systemic symptoms, rashes, transient hyperphosphatasemia, neutropenia, eosinophilia and elevations in serum transaminases, in up to 10% of cases.[137-140, 144-146, 148, 208]

Recommendations of Other Groups

The CDC updated its lead screening recommendations in 1997 in response to evidence of inadequate screening of children at high risk, and to concerns regarding appropriate use of limited resources in low prevalence communities. The revised CDC guidelines provided state public health entities with authority and guidance to develop state and local policies for childhood lead screening. The CDC recommended universal screening in communities without data regarding the prevalence of elevated blood lead levels adequate for local policy development, and in communities where ≥27% of the housing was built before 1950. Screening of all children receiving Medicaid, Supplemental Food Program for Women, Infants and Children (WIC) or other governmental assistance, and in populations where ≥12% of children ages 1-2 years have elevated blood lead levels was also recommended. Targeted screening is recommended for all other children based on individual risk assessment.[27] This approach is also supported by the American College of Preventive Medicine.[209]

The American Academy of Pediatrics recommends that pediatricians:

(1) Provide anticipatory guidance to parents of all infants and children regarding potential risk factors and specific prevention strategies tailored for the family and community.
(2) In conjunction with public health authorities, develop and use community-specific risk assessment questionnaires to guide targeted screening in communities where universal screening is not appropriate.
(3) Provide lead screening at age 9-12 months and consider again at ~24 months following state health department guidelines utilizing individualized targeted or universal screening as recommended.
(4) Assess possible lead exposure periodically between 6 months and 6 years of age using community-specific risk assessment questionnaires. Blood lead testing should be considered in children with a history of abuse, neglect, or conditions associated with increased lead exposure.
(5) Actively participate in state and local lead poisoning prevention activities.

Recommendations by the AAP regarding the urgency and extent of follow-up differ slightly from those of the CDC, and depend on the risk classification and on confirmed venous blood lead levels.[210]

The American Academy of Family Physicians (AAFP) recommends lead screening at 12 months of age in infants who have the following risk factors:

- residence in a community with a high or undefined prevalence of lead levels requiring intervention,
- residence in or frequent visits to a home built before 1950 that has dilapidated paint or has recently undergone or is undergoing renovation or remodeling,
- close contact to a person who has an elevated blood lead level,
- residence near a lead industry or heavy traffic,
- residence with a person whose hobby or job involves lead exposure,
- use of lead-based pottery,
- or use of traditional remedies that contain lead.[211]

Medicaid's Early and Periodic Screening, Diagnostic, and Treatment Program requires that all children be considered at risk and must be screened for lead poisoning. CMS requires that all children receive a screening blood lead test at 12 months and 24 months of age. Children between the ages of 36 months and 72 months of age must receive a screening blood lead test if they have not been previously screened for lead poisoning. At this time states may not adopt a statewide plan for screening children for lead poisoning that does not require lead screening for all Medicaid-eligible children.[5, 212]

Studies of provider behavior before and after the 1997 Revision of the CDC Recommendations demonstrate that blood lead screening and follow-up of children is often inadequate.[213, 214]

Recently, the CDC Advisory Committee on Childhood Lead Poisoning Prevention (ACCLPP) reaffirmed its support for state and local decision making based on local data and conditions regarding the appropriate lead screening recommendations. The ACCLPP also acknowledged the limitations of screening and other forms of secondary prevention, and advocated a increased local and national focus on housing-based primary prevention of lead exposure.[29]

No national organizations currently recommend screening pregnant women for elevated lead levels. Some state organizations have developed local policies regarding lead screening. In 1995, the New York State Department of Health and American College of Obstetricians and Gynecologists District II developed lead poisoning prevention guidelines that mandate anticipatory guidance for pregnant women, risk assessment, and risk reduction counseling and childhood lead poisoning prevention education.[215]

Discussion

A summary of the evidence for each key question addressed in the evidence synthesis is provided in Table 6. There is fair evidence that screening for elevated lead levels in asymptomatic children at increased risk for lead exposure will improve clinical outcomes. Because there have been no controlled trials directly evaluating screening for elevated lead levels, this conclusion is based on a chain of evidence constructed from studies of weaker design. First, in young asymptomatic children, blood lead levels as low as 10 micro-g/dL and perhaps lower are associated with measurable neurodevelopmental dysfunction. Second, although the national prevalence of elevated lead levels has declined substantially in the past two decades, a high prevalence persists in some communities, particularly poor urban communities in the Northeast and Midwest U.S. Third, measurement of venous blood lead concentration is a reliable, precise and reasonably valid screening test for assessing lead exposure. Fourth, current interventions, including residential lead hazard control and chelation therapy, can reduce blood lead levels in children identified with levels ≥25 micro-g/dL, although the quality of evidence supporting their effectiveness is weak and a beneficial effect on IQ or other clinical outcomes has not yet been demonstrated. Well-designed randomized controlled trials do not support beneficial effects of chelation therapy for asymptomatic children with levels <45 micro-g/dL. There is also weak evidence that screening high-risk children for elevated lead levels results in improved clinical outcome compared to historical controls identified by case finding. Based on this evidence of the current burden of suffering and the effectiveness of early detection, the Task Force recommends screening children at increased risk for lead exposure.

While no studies have evaluated a specific age at which to screen, the natural history of blood lead levels in children, which increase most rapidly between 6 and 12 months and peak at age 18-24 months, suggests that screening at about 12 months of age is likely to be most effective for the early detection of elevated lead levels.

For those children who are screened and found to have initial blood lead levels <25 micro-g/dL, there is as yet little evidence regarding the effectiveness of early detection and intervention, or of repeated screening to detect further increases in blood lead. Longitudinal and cross-sectional

studies suggest that in children ≥2 years, most such levels will decline naturally with time, but elevated levels may persist in children who are chronically exposed.

There is no direct evidence comparing the outcomes of universal screening with the outcomes from targeted screening for elevated lead levels. Recent studies indicate that the prevalence of elevated blood levels in the U.S. has declined dramatically in the past two decades, but local prevalence is highly variable, with more than tenfold differences between communities. In a community with a low prevalence of elevated blood lead levels, universal screening may result in disproportionate risks and costs relative to benefits. The prevalence level at which targeted screening can replace universal screening is a public health policy decision requiring consideration of factors in addition to the scientific evidence for effectiveness of early detection, such as available resources, competing public health needs, and costs and availability of alternative approaches to reducing lead exposure. Clinicians can consult with their local or state health department regarding appropriate screening policy for the local child population.

In communities where data suggest that universal screening is not indicated, there may nevertheless be some children who are at increased risk of blood lead levels in the range for which individual intervention by chelation therapy or residential lead hazard control has been demonstrated to be effective. In addition to risks from housing, these children may have had exposure to other lead sources such as lead-based hobbies or industries, traditional ethnic remedies, or lead-based pottery. Selective blood lead screening of such high-risk children is appropriate even in low prevalence communities. There is fair evidence that a validated questionnaire of known and acceptable sensitivity and specificity can identify those at high risk. In several studies, the CDC[124] and similar questionnaires correctly identified 64% to 87% of urban and suburban children who had blood lead levels ≥10 micro-g/dL. These questionnaires have not been adequately evaluated as a screening tool to detect higher blood lead levels (e.g., ≥20-25 micro-g/dL), or to detect exposure in other populations (e.g., migrant workers, rural communities). Locale-specific questionnaires that inquire about likely local sources of lead exposure may lead to improved prediction.

As is the case in children, there are no controlled trials evaluating screening for elevated lead levels in pregnant women, nor are there sufficient data to construct an adequate chain of evidence demonstrating benefit. The prevalence of levels >15 micro-g/dL appears to be quite low in pregnant women. There is fair evidence that mildly elevated lead levels during pregnancy are associated with small increases in antepartum blood pressure, but limited evidence that these levels have important adverse effects on reproductive or other outcomes, including intelligence of offspring. An extensive literature search failed to identify studies evaluating screening or intervention for lead exposure in pregnant women. There are potentially important adverse effects of chelation therapy on the fetus and of residential lead hazard control on both the pregnant woman and fetus if they are not performed according to established standards. Removal to a lead-free environment would theoretically be effective in reducing lead exposure but has not been specifically evaluated in pregnancy. There is thus insufficient evidence to recommend for or against screening pregnant women for the detection of elevated lead levels.

Community-based interventions for the primary prevention of lead exposure are likely to be more effective, and may be more cost-effective, than office-based screening, treatment and

counseling.[29] Community, regional, and national environmental lead hazard reduction efforts, such as reducing lead in industrial emissions, gasoline, and cans, have proven highly effective in reducing population blood lead levels.[216-223] Remaining important sources of lead (e.g., lead paint and pipes in older homes, lead-contaminated soil) are, however, more difficult to address on a population-wide basis. Studies of community-based efforts to reduce lead exposure from these and other sources in order to prevent the occurrence of elevated lead levels are ongoing.[23, 158, 224] Evaluation of the effectiveness of community-based interventions, and recommendations regarding their use, are beyond the scope of this document.

References

1. DiGuiseppi C. Screening for Elevated Lead Levels in Childhood and Pregnancy. *Guide to Clinical Preventive Services: Report of the U. S. Preventive Services Task Force*. 2nd ed. Baltimore: Williams & Wilkins; 1996.
2. U. S. Preventive Services Task Force. Screening for Elevated Lead Levels in Childhood and Pregnancy: Recommendation. *Guide to Clinical Preventive Services: Report of the U. S. Preventive Services Task Force*. 2nd ed. Baltimore: Williams & Wilkins; 1996.
3. Harris RP, Helfand M, Woolf SH, et al. Current methods of the US Preventive Services Task Force. A review of the process. *Am J Prev Med.* 2001;30(3S):21-35.
4. Bellinger DC, Hu H, Kalaniti K, et al. A pilot study of blood lead levels and neurobehavioral function in children living in Chennai, India. *Int J Occup Environ Health.* 2005;11(2):138-143.
5. Centers for Disease Control and Prevention. Blood Lead Levels - United States, 1999-2002. *MMWR.* 2005;54(20):513-516.
6. Brody DJ, Pirkle JL, Kramer RA, et al. Blood lead levels in the US population. Phase 1 of the Third National Health and Nutrition Examination Survey (NHANES III, 1988 to 1991) [erratum appears in JAMA 1995 Jul 12;274(2):130]. *JAMA.* 1994;272(4):277-283.
7. Fredeen DJ, Ehlinger EP, Cruikshank SH, Godes JR, Braun JE, Deinard AS. Lead levels among pregnant women in Hennepin County. *Minnesota Medicine.* 1992;75(11):29-32.
8. Flanigan GD, Jr., Mayfield R, Blumenthal HT. Studies on lead exposure in patients of a neighborhood health center: Part II. A comparison of women of childbearing age and children. *J Nat Med Assoc.* 1992;84(1):23-27.
9. Stefanak MA, Bourguet CC, Benzies-Styka T. Use of the Centers for Disease Control and Prevention childhood lead poisoning risk questionnaire to predict blood lead elevations in pregnant women. *Obstet Gynecol.* 1996;87(2):209-212.
10. Crocetti AF, Mushak P, Schwartz J. Determination of numbers of lead-exposed women of childbearing age and pregnant women: An integrated summary of a report to the U.S. Congress on childhood lead poisoning. *Environ Health Perspect.* 1990;89:121-124.
11. Rhainds M, Levallois P, Dewailly E, Ayotte P. Lead, mercury, and organochlorine compound levels in cord blood in Quebec, Canada. *Arch Environ Health.* 1999;54(1):40-47.
12. Lee MG, Chun OK, Song WO. Determinants of the blood lead level of US women of reproductive age. *J Am Coll Nutr.* 2005;24(1):1-9.
13. Hu H, Hashimoto D, Besser M. Levels of lead in blood and bone of women giving birth in a Boston hospital. *Arch Environ Health.* 1996;51(1):52-58.
14. Needleman H. Lead poisoning. *Annu Rev Med.* 2004;55:209-222.
15. Centers for Disease Control and Prevention. Elevated blood lead levels in refugee children: New Hampshire, 2003-2004. *MMWR.* 2005;54(2):42-46.
16. centers for Disease Control and Prevention. CDC Recommendations for Lead Poisoning Prevention in Newly Arrived Refugee Children. Added 6.8.05; www.cdc.gov/nceh/lead/refugee%20recs.htm. Accessed June 2, 2005, 2005.

17. Surveillance for elevated blood lead levels among children: United States, 1997-2001. *MMWR.* 2003;52(SS10):1-21.
18. From the Centers for Disease Control and Prevention. Blood lead levels in young children--United States and selected states, 1996-1999. *JAMA.* 2001;285(3):286-287.
19. Children with elevated blood lead levels attributed to home renovation and remodeling activities--New York, 1993-1994. *MMWR.* 1997;45(51-52):1120-1123.
20. Sargent JD, Brown MJ, Freeman JL, Bailey A, Goodman D, Freeman DH, Jr. Childhood lead poisoning in Massachusetts communities: its association with sociodemographic and housing characteristics. *Am J Public Health.* 1995;85(4):528-534.
21. Committee on Measuring Lead in Critical Populations NRC. Measuring lead exposure in infants, children, and other sensitive populations. *Washington DC: National Academy Press.* 1993.
22. Agency for Toxic Substances and Disease Registry. The nature and extent of lead poisoning in children in the United States: a report to Congress. *Atlanta: Department of Health and Human Services.* 1988;Publication no. DHHS-99-2966.
23. Department of Housing and Urban Development. Comprehensive and workable plan for the abatement of lead-based paint in privately owned housing. *Report to Congress. Washington, DC.* 1990;Publication no. HUD-PDR-1295.
24. Environmental Protection Agency. Reducing lead in drinking water: a benefit analysis. *Washington, DC: Environmental Protection Agency.* 1986;Office of Policy Planning and Evaluation.
25. Arnetz BB, Nicolich MJ. Modeling of environmental lead contributors to blood lead in human. *Int Arch Occup Environ Health.* 1990;62(5):397-402.
26. Jacobs DE, Clickner RP, Zhou JY, et al. The prevalence of lead-based paint hazards in U.S. housing. *Environ Health Perspect.* 2002;110(10).
27. Centers for Disease Control and Prevention NCfEH. *Screening young children for lead poisoning: guidance for state and local health officials.* Atlanta, GA: USDHHS; 1997.
28. Centers for Disease Control and Prevention Advisory Committee on Childhood Lead Poisoning. Recommendations for blood lead screening of young children enrolled in Medicaid: targeting a group at high risk. *MMWR.* 2000;49(RR-14):1-13.
29. Centers for Disease Control and Prevention Advisory Committee on Childhood Lead Poisoning. *Preventing Lead Exposure in Young Children: A Housing-Based Approach to Primary Prevention of Lead Poisoning.* Atlanta, GA: U. S. DHHS; 2004.
30. Centers for Disease C, Prevention. Blood lead levels in residents of homes with elevated lead in tap water--District of Columbia, 2004. *MMWR..* 2004;53(12):268-270.
31. Gardella C. Lead exposure in pregnancy: a review of the literature and argument for routine prenatal screening. *Obstet Gynecol Surv.* 2001;56(4):231-238.
32. Rhainds M, Levallois P. Effects of maternal cigarette smoking and alcohol consumption on blood lead levels of newborns. *Am J Epidemiol.* 1997;145(3):250-257.
33. Harville EW, Hertz-Picciotto I, Schramm M, et al. Factors influencing the difference between maternal and cord blood lead. *Occup Environ Med.* 2005;62(4):263-269.
34. Klitzman S, Sharma A, Nicaj L, Vitkevich R, Leighton J. Lead poisoning among pregnant women in New York City: risk factors and screening practices. *J Urban Health.* 2002;79(2):225-237.
35. Lanphear BP, Dietrich KN, Berger O. Prevention of lead toxicity in US children. *Ambul Pediatr.* 2003;3(1):27-36.

36. Fatal pediatric lead poisoning--New Hampshire, 2000. *MMWR.* 2001;50(22):457-459.
37. Baghurst PA, McMichael AJ, Wigg NR, et al. Environmental exposure to lead and children's intelligence at the age of seven years. The Port Pirie Cohort Study. *N Engl J Med.* 1992;327(18):1279-1284.
38. Cooney G, Bell A, Stravou C. Low level exposure to lead and neurobehavioural development: the Sydney Study at seven years. *Proceedings of Heavy Metals in the Environment Conference, Edinburgh.* 1991;Farmer JG, ed.(1):16-19.
39. Bellinger DC, Stiles KM, Needleman HL. Low-level lead exposure, intelligence and academic achievement: a long-term follow-up study. *Pediatrics.* 1992;90(6):855-861.
40. Dietrich KN, Berger OG, Succop PA, Hammond PB, Bornschein RL. The developmental consequences of low to moderate prenatal and postnatal lead exposure: intellectual attainment in the Cincinnati Lead Study Cohort following school entry. *Neurotoxicol Teratol.* 1993;15(1):37-44.
41. Ernhart CB, Morrow-Tlucak M, Wolf AW, Super D, Drotar D. Low level lead exposure in the prenatal and early preschool periods: intelligence prior to school entry. *Neurotoxicol Teratol.* 1989;11(2):161-170.
42. Wasserman GA, Graziano JH, Factor-Litvak P, et al. Consequences of lead exposure and iron supplementation on childhood development at age 4 years. *Neurotoxicol Teratol.* 1994;16(3):233-240.
43. Wolf AW, Jimenez E, Lozoff B. No evidence of developmental III effects of low-level lead exposure in a developing country. *J Dev Behav Pediatr.* 1994;15(4):224-231.
44. Pocock SJ, Smith M, Baghurst P. Environmental lead and children's intelligence: a systematic review of the epidemiological evidence. *BMJ.* 1994;309(6963):1189-1197.
45. Chen A, Dietrich K, Ware JH, Radcliffe J, Rogan W. IQ and blood lead from 2 to 7 years of age: are the effects in older children the residual of high blood lead concentrations in 2-year-olds? *Environ Health Perspect.* 2005;113(5):597-601.
46. Needleman HL, Gatsonis CA. Low-level lead exposure and the IQ of children. A meta-analysis of modern studies. *JAMA.* 1990;263(5):673-678.
47. Winneke G, Brockhaus A, Ewers U, Kramer U, Neuf M. Results from the European multicenter study on lead neurotoxicity in children: implications for risk assessment. *Neurotoxicol Teratol.* 1990;12(5):553-559.
48. Winneke G, Beginn U, Ewert T, et al. Comparing the effects of perinatal and later childhood lead exposure on neuropsychological outcome. *Environ Res.* 1985;38(1):155-167.
49. Winneke G, Kramer U, Brockhaus A, et al. Neuropsychological studies in children with elevated tooth-lead concentrations. II. Extended study. *Int Arch Occup Environ Health.* 1983;51(3):231-252.
50. Winneke G, Brockhaus A, Collet W, Kramer U. Modulation of lead-induced performance deficit in children by varying signal rate in a serial choice reaction task. *Neurotoxicol Teratol.* 1989;11(6):587-592.
51. Hatzakis A, Kokkevi A, Katsouyanni K, al. e. Psychometric intelligence and attentional performance deficits in lead-exposed children. *Proceedings of the International Conference: heavy metals in the environment.* 1987;1:204-209.
52. Wigg NR. Low-level lead exposure and children. *J Paediatr Child Health.* 2001;37(5):423-425.
53. Bellinger DC. Lead. *Pediatrics.* 2004;113(4 Suppl):1016-1022.

54. Otto DA, Fox DA. Auditory and visual dysfunction following lead exposure. *Neurotoxicology.* 1993;14(2-3):191-207.
55. Cory-Slechta D. The behavioral toxicity of lead: problems and perspectives. *Adv Behav Pharmacol.* 1984;4:211-255.
56. Rice D. Lead-induced changes in learning: evidence for behavioral mechanisms from experimental animal studies. *Neurotoxicology.* 1993;14:167-178.
57. Koller K, Brown T, Spurgeon A, Levy L. Recent developments in low-level lead exposure and intellectual impairment in children. *Environ Health Perspect.* 2004;112(9):987-994.
58. Canfield RL, Gendle MH, Cory-Slechta DA. Impaired neuropsychological functioning in lead-exposed children. *Dev Neuropsychol.* 2004;26(1):513-540.
59. Lanphear BP, Dietrich K, Auinger P, Cox C. Cognitive deficits associated with blood lead concentrations <10 microg/dL in US children and adolescents. *Public Health Rep.* 2000;115(6):521-529.
60. Chiodo LM, Jacobson SW, Jacobson JL. Neurodevelopmental effects of postnatal lead exposure at very low levels. *Neurotoxicol Teratol.* 2004;26(3):359-371.
61. Lanphear B, Hornung R, Khoury J, al. e. Low-level environmental lead exposure and children's intellectual function: an international pooled analysis. *Environ Health Perspect.* 2005;113:894-899.
62. Ernhart CB, Wolf AW, Kennard MJ, Erhard P, Filipovich HF, Sokol RJ. Intrauterine exposure to low levels of lead: the status of the neonate. *Arch Environ Health.* 1986;41(5):287-291.
63. McMichael AJ, Vimpani GV, Robertson EF, Baghurst PA, Clark PD. The Port Pirie cohort study: maternal blood lead and pregnancy outcome. *J Epidemiol Community Health.* 1986;40(1):18-25.
64. Bellinger D, Leviton A, Rabinowitz M, Allred E, Needleman H, Schoenbaum S. Weight gain and maturity in fetuses exposed to low levels of lead. *Environ Res.* 1991;54(2):151-158.
65. Murphy MJ, Graziano JH, Popovac D, et al. Past pregnancy outcomes among women living in the vicinity of a lead smelter in Kosovo, Yugoslavia. *Am J Public Health.* 1990;80(1):33-35.
66. Lindbohm ML, Sallmen M, Anttila A, Taskinen H, Hemminki K. Paternal occupational lead exposure and spontaneous abortion. *Scand J Work Environ Health.* 1991;17(2):95-103.
67. Laudanski T, Sipowicz M, Modzelewski P, et al. Influence of high lead and cadmium soil content on human reproductive outcome. *Int J Gynaecol Obstet.* 1991;36(4):309-315.
68. Dietrich KN, Krafft KM, Bornschein RL, et al. Low-level fetal lead exposure effect on neurobehavioral development in early infancy. *Pediatrics.* 1987;80(5):721-730.
69. Factor-Litvak P, Graziano JH, Kline JK, et al. A prospective study of birth weight and length of gestation in a population surrounding a lead smelter in Kosovo, Yugoslavia. *Int J Epidemiol.* 1991;20(3):722-728.
70. Milman N, Christensen JM, Ibsen KK. Blood lead and erythrocyte zinc protoporphyrin in mothers and newborn infants. *Eur J Pediatr.* 1988;147(1):71-73.
71. Ernhart CB. A critical review of low-level prenatal lead exposure in the human: 1. Effects on the fetus and newborn. *Reprod Toxicol.* 1992;6(1):9-19.

72. Baghurst PA, Robertson EF, Oldfield RK, et al. Lead in the placenta, membranes, and umbilical cord in relation to pregnancy outcome in a lead-smelter community. *Environ Health Perspect.* 1991;90:315-320.
73. Andrews KW, Savitz DA, Hertz-Picciotto I. Prenatal lead exposure in relation to gestational age and birth weight: a review of epidemiologic studies. *Am J Ind Med.* 1994;26(1):13-32.
74. Rothenberg SJ, Schnaas L, Perroni E, Hernandez RM, Martinez S, Hernandez C. Pre- and postnatal lead effect on head circumference: a case for critical periods. *Neurotoxicol Teratol.* 1999;21(1):1-11.
75. Gonzalez-Cossio T, Peterson KE, Sanin LH, et al. Decrease in birth weight in relation to maternal bone-lead burden. *Pediatrics.* 1997;100(5):856-862.
76. Emory E, Pattillo R, Archibold E, Bayorh M, Sung F. Neurobehavioral effects of low-level lead exposure in human neonates. *Am J Obstet Gynecol.* 1999;181(1).
77. Emory E, Ansari Z, Pattillo R, Archibold E, Chevalier J. Maternal blood lead effects on infant intelligence at age 7 months. *Am J Obstet Gynecol.* 2003;188(4).
78. Rothenberg SJ, Poblano A, Schnaas L. Brainstem auditory evoked response at five years and prenatal and postnatal blood lead. *Neurotoxicol Teratol.* 2000;22(4):503-510.
79. Rothenberg SJ, Schnaas L, Salgado-Valladares M, et al. Increased ERG a- and b-wave amplitudes in 7- to 10-year-old children resulting from prenatal lead exposure. *Invest Ophthalmol Vis Sci.* 2002;43(6):2036-2044.
80. Chisolm JJ, Jr. The use of chelating agents in the treatment of acute and chronic lead intoxication in childhood. *J Pediatr.* 1968;73(1):1-38.
81. Pueschel SM, Kopito L, Schwachman H. Children with an increased lead burden. A screening and follow-up study. *JAMA.* 1972;222(4):462-466.
82. Nuyts GD, Daelemans RA, Jorens PG, Elseviers MM, Van de Vyver FL, De Broe ME. Does lead play a role in the development of chronic renal disease? *Nephrol Dial Transplant.* 1991;6(5):307-315.
83. Hu H. A 50-year follow-up of childhood plumbism. Hypertension, renal function, and hemoglobin levels among survivors. *Am J Dis Child.* 1991;145(6):681-687.
84. Bernard AM, Vyskocil A, Roels H, Kriz J, Kodl M, Lauwerys R. Renal effects in children living in the vicinity of a lead smelter. *Environ Res.* 1995;68(2):91-95.
85. Fels LM, Wunsch M, Baranowski J, et al. Adverse effects of chronic low level lead exposure on kidney function--a risk group study in children. *Nephrol Dial Transplant.* 1998;13(9):2248-2256.
86. Grandjean P, Hollnagel H, Hedegaard L, Christensen JM, Larsen S. Blood lead-blood pressure relations: alcohol intake and hemoglobin as confounders. *Am J Epidemiol.* 1989;129(4):732-739.
87. Elwood PC, Yarnell JW, Oldham PD, et al. Blood pressure and blood lead in surveys in Wales. *Am J Epidemiol.* 1988;127(5):942-945.
88. Schwartz J. Lead, blood pressure, and cardiovascular disease in men and women. *Environ Health Perspect.* 1991;91:71-75.
89. Moller L, Kristensen TS. Blood lead as a cardiovascular risk factor. *Am J Epidemiol.* 1992;136(9):1091-1100.
90. Dolenc P, Staessen JA, Lauwerys RR, Amery A. Short report: low-level lead exposure does not increase the blood pressure in the general population. Cadmibel Study Group. *J Hypertens.* 1993;11(5):589-593.

91. Hense HW, Filipiak B, Keil U. The association of blood lead and blood pressure in population surveys. *Epidemiology.* 1993;4:173-179.
92. Rabinowitz M, Bellinger D, Leviton A, Needleman H, Schoenbaum S. Pregnancy hypertension, blood pressure during labor, and blood lead levels. *Hypertension.* 1986;10(4):447-451.
93. Selbst SM, Sokas RK, Henretig FM, Weller SC, Tershakovec AM. The effect of blood lead on blood pressure in children. *J Environ Pathol Toxicol Oncol.* 1993;12(4):213-218.
94. Schwartz J, Angle C, Pitcher H. Relationship between childhood blood lead levels and stature. *Pediatrics.* 1986;77(3):281-288.
95. Frisancho AR, Ryan AS. Decreased stature associated with moderate blood lead concentrations in Mexican-American children. *Am J Clin Nutr.* 1991;54(3):516-519.
96. Shukla R, Dietrich KN, Bornschein RL, Berger O, Hammond PB. Lead exposure and growth in the early preschool child: a follow-up report from the Cincinnati Lead Study. *Pediatrics.* 1991;88(5):886-892.
97. Greene T, Ernhart CB. Prenatal and preschool age lead exposure: relationship with size. *Neurotoxicol Teratol.* 1991;13(4):417-427.
98. Rothenberg SJ, Manalo M, Jiang J, et al. Blood lead level and blood pressure during pregnancy in South Central Los Angeles. *Arch Environ Health.* 1999;54(6):382-389.
99. Rothenberg SJ, Kondrashov V, Manalo M, et al. Increases in hypertension and blood pressure during pregnancy with increased bone lead levels. *Am J Epidemiol.* 2002;156(12):1079-1087.
100. Magri J, Sammut M, Savona-Ventura C. Lead and other metals in gestational hypertension. *Int J Gynaecol Obstet.* 2003;83(1):29-36.
101. Dawson EB, Evans DR, Kelly R, Van Hook JW. Blood cell lead, calcium, and magnesium levels associated with pregnancy-induced hypertension and preeclampsia. *Biol Trace Elem Res.* 2000;74(2):107-116.
102. Jacobson BE, Lockitch G, Quigley G. Improved sample preparation for accurate determination of low concentrations of lead in whole blood by graphite furnace analysis. *Clin Chem.* 1991;37(4):515-519.
103. Parsons P, Raciti KA, Esernio-Jenssen D. Evaluation and improvement of sample collection procedures for the determination of blood lead. *Third semi-annual report to the Center for Environmental Health and Injury Control.* 1993;Center for Disease Control and Prevention(Atlanta: Centers for Disease Control and Prevention).
104. Schlenker TL, Fritz CJ, Mark D, et al. Screening for pediatric lead poisoning. Comparability of simultaneously drawn capillary and venous blood samples. *JAMA.* 1994;271(17):1346-1348.
105. Schonfeld DJ, Cullen MR, Rainey PM, et al. Screening for lead poisoning in an urban pediatric clinic using samples obtained by fingerstick. *Pediatrics.* 1994;94(2 Pt 1):174-179.
106. Lyngbye T, Jorgensen PJ, Grandjean P, Hansen ON. Validity and interpretation of blood lead levels: a study of Danish school children. *Scand J Clin Lab Invest.* 1990;50(4):441-449.
107. Schonfeld DJ, Rainey PM, Cullen MR, Showalter DR, Cicchetti DV. Screening for lead poisoning by fingerstick in suburban pediatric practices. *Arch Pediatr Adolesc Med.* 1995;149(4):447-450.

108. Parsons PJ. Monitoring human exposure to lead: an assessment of current laboratory performance for the determination of blood lead. *Environ Res.* 1992;57(2):149-162.
109. Blumenthal HT, Flanigan GD, Jr., Mayfield R. Studies on lead exposure in patients of a neighborhood health center: Part I: Pediatric patients. *J Natl Med Assoc.* 1991;83:1065-1072.
110. Mahaffey KR, Annest JL. Association of erythrocyte protoporphyrin with blood lead level and iron status in the second National Health and Nutrition Examination Survey, 1976-1980. *Environ Res.* 1986;41(1):327-338.
111. Debaun MR, Sox HC. Setting the optimal erythrocyte protoporphyrin screening decision threshold for lead poisoning: a decision analytic approach. *Pediatrics.* 1991;88:121-131.
112. Parsons PJ, Reilly AA, Hussain A. Observational study of erythrocyte protoporphyrin screening test for detecting low lead exposure in children: impact of lowering the blood lead action threshold. *Clin Chem.* 1991;37(2):216-225.
113. McElvaine MD, Orbach HG, Binder S, Blanksma LA, Maes EF, Krieg RM. Evaluation of the erythrocyte protoporphyrin test as a screen for elevated blood lead levels. *J Pediatr.* 1991;119(4):548-550.
114. Leung FY, Bradley C, Pellar TG. Reference intervals for blood lead and evaluation of zinc protoporphyrin as a screening test for lead toxicity. *Clin Biochem.* 1993;26(6):491-496.
115. Rolfe PB, Marcinak JF, Nice AJ, Williams RH. Use of zinc protoporphyrin measured by the Protofluor-Z hematofluorometer in screening children for elevated blood lead levels. *Am J Dis Child.* 1993;147(1):66-68.
116. Marcus AH, Schwartz J. Dose-response curves for erythrocyte protoporphyrin vs. blood lead: effects of iron status. *Environ Res.* 1987;44(2):221-227.
117. Guthrie R, Orfanos A, Widger K, Luskin B, Francemone C, Nadler D. Screening suburban/rural children for lead exposure, iron deficiency. *Am J Public Health.* 1988;78(7):856-857.
118. Tejeda DM, Wyatt DD, Rostek BR, Solomon WB. Do questions about lead exposure predict elevated lead levels? *Pediatrics.* 1994;93(2):192-194.
119. Binns HJ, LeBailly SA, Poncher J, Kinsella TR, Saunders SE. Is there lead in the suburbs? Risk assessment in Chicago suburban pediatric practices. Pediatric Practice Research Group. *Pediatrics.* 1994;93(2):164-171.
120. Nordin JD, Rolnick SJ, Griffin JM. Prevalence of excess lead absorption and associated risk factors in children enrolled in a Midwestern health maintenance organization. *Pediatrics.* 1994;93(2):172-177.
121. Schaffer SJ, Szilagyi PG, Weitzman M. Lead poisoning risk determination in an urban population through the use of a standardized questionnaire. *Pediatrics.* 1994;93(2):159-163.
122. Rooney BL, Hayes EB, Allen BK, Strutt PJ. Development of a screening tool for prediction of children at risk for lead exposure in a Midwestern clinical setting. *Pediatrics.* 1994;93(2):183-187.
123. Striph KB. Prevalence of lead poisoning in a suburban practice. *J Fam Pract.* 1995;41(1):65-71.
124. Centers for Disease Control and Prevention. *Preventing lead poisoning in young children. A statement by the Centers for Disease Control - October 1991.* Atlanta: Department of Health and Human Services; 1991.

125. France EK, Gitterman BA, Melinkovich P, Wright RA. The accuracy of a lead questionnaire in predicting elevated pediatric blood lead levels. *Arch Pediatr Adolesc Med.* 1996;150(9):958-963.
126. Kazal LA, Jr. The failure of CDC screening questionnaire to efficiently detect elevated lead levels in a rural population of children. *J Fam Pract.* 1997;45(6):515-518.
127. Muniz MA, Dundas R, Mahoney MC. Evaluation of a childhood lead questionnaire in predicting elevated blood lead levels in a rural community. *J Rural Health.* 2003;19(1):15-19.
128. Robin LF, Beller M, Middaugh JP. Statewide assessment of lead poisoning and exposure risk among children receiving Medicaid services in Alaska. *Pediatrics.* 1997;99(4).
129. Schaffer SJ, Kincaid MS, Endres N, Weitzman M. Lead poisoning risk determination in a rural setting. *Pediatrics.* 1996;97(1):84-90.
130. Sargent JD, Dalton M, Klein RZ. Diagnostic testing unwarranted for children with blood lead 10 to 14 microg/dL. *Pediatrics.* 1999;103(4).
131. Lanphear B, Hornung R, Ho M. Screening housing to prevent lead toxicity in children. . *Public Health Rep.* 2005;120:305-310.
132. McCusker J. Longitudinal changes in blood lead level in children and their relationship to season, age, and exposure to paint or plaster. *Am J Public Health.* 1979;69(4):348-352.
133. Reigart JR, Whitlock NH. Longitudinal observations of the relationship between free erythrocyte porphyrins and whole blood lead. *Pediatrics.* 1976;57(1):54-59.
134. Sachs HK, Blanksma LA, Murray EF, O'Connell MJ. Ambulatory treatment of lead poisoning: report of 1,155 cases. *Pediatrics.* 1970;46(3):389-396.
135. Sachs HK. Effect of a screening program on changing patterns of lead poisoning. *Environ Health Perspect.* 1974;7:41-45.
136. Browder A, Joselow M, Louria DB, Lavenhar M, Foster J. Evaluation of screening programs for childhood lead poisoning by analysis of hospital admissions. *Am J Public Health.* 1974;64(9):914-915.
137. Rogan W. The Treatment of Lead-exposed Children (TLC) trial: design and recruitment for a study of the effect of oral chelation on growth and development in toddlers. *Paediatr Perinat Epidemiol.* 1998;12:313-333.
138. Rogan WJ, Dietrich KN, Ware JH, et al. The effect of chelation therapy with succimer on neuropsychological development in children exposed to lead. *N Engl J Med.* 2001;344(19):1421-1426.
139. Liu X, Dietrich KN, Radcliffe J, Ragan NB, Rhoads GG, Rogan WJ. Do children with falling blood lead levels have improved cognition? *Pediatrics.* 2002;110(4):787-791.
140. Dietrich KN, Ware JH, Salganik M, et al. Effect of chelation therapy on the neuropsychological and behavioral development of lead-exposed children after school entry. *Pediatrics.* 2004;114(1):19-26.
141. Peterson KE, Salganik M, Campbell C, et al. Effect of succimer on growth of preschool children with moderate blood lead levels. *Environ Health Perspect.* 2004;112(2):233-237.
142. Ruff HA, Bijur PE, Markowitz M, Ma YC, Rosen JF. Declining blood lead levels and cognitive changes in moderately lead-poisoned children. *JAMA.* 1993;269(13):1641-1646.

143. Markowitz ME, Bijur PE, Ruff H, Rosen JF. Effects of calcium disodium versenate (CaNa2EDTA) chelation in moderate childhood lead poisoning. *Pediatrics.* 1993;92(2):265-271.
144. Rogan W. Safety and efficacy of succimer in toddlers with blood lead levels of 20-44 ug/dL. *Pediatr Res.* 2000;48(5):593-599.
145. Graziano JH, Lolacono NJ, Moulton T, Mitchell ME, Slavkovich V, Zarate C. Controlled study of meso-2,3-dimercaptosuccinic acid for the management of childhood lead intoxication. *J Pediatr.* 1992;120(1):133-139.
146. Graziano JH, Lolacono NJ, Meyer P. Dose-response study of oral 2,3-dimercaptosuccinic acid in children with elevated blood lead concentrations. *J Pediatr.* 1988;113(4):751-757.
147. Shannon M, Graef J, Lovejoy FH, Jr. Efficacy and toxicity of D-penicillamine in low-level lead poisoning. *J Pediatr.* 1988;112(5):799-804.
148. Liebelt EL, Shannon M, Graef JW. Efficacy of oral meso-2,3-dimercaptosuccinic acid therapy for low-level childhood plumbism. *J Pediatr.* 1994;124(2):313-317.
149. Shannon M, Grace A, Graef JW. Use of penicillamine in children with small lead burdens. *N Engl J Med.* 1989;321(14):979-980.
150. Besunder JB, Anderson RL, Super DM. Short-term efficacy of oral dimercaptosuccinic acid in children with low to moderate lead intoxication. *Pediatrics.* 1995;96(4 Pt 1):683-687.
151. O'Connor ME, Rich D. Children with moderately elevated lead levels: is chelation with DMSA helpful? *Clin Pediatr.* 1999;38(6):325-331.
152. Chisolm JJ, Jr. Safety and efficacy of meso-2,3-dimercaptosuccinic acid (DMSA) in children with elevated blood lead concentrations. *J Toxicol Clin Toxicol.* 2000;38(4):365-375.
153. Moel DI, Sachs HK, Drayton MA. Slow, natural reduction in blood lead level after chelation therapy for lead poisoning in childhood. *Am J Dis Child.* 1986;140(9):905-908.
154. Chisolm JJ, Jr. Chelation therapy in children with subclinical plumbism. *Pediatrics.* 1974;53(3):441-443.
155. Vitale LF, Rosalinas-Bailon A, Folland D, Brennan JF, McCormick B. Oral penicillamine therapy for chronic lead poisoning in children. *J Pediatr.* 1973;83(6):1041-1045.
156. Marcus SM. Experience with D-penicillamine in treating lead poisoning. *Vet Hum Toxicol.* 1982;24(1):18-20.
157. Markowitz ME, Bijur PE, Ruff HA, Balbi K, Rosen JF. Moderate lead poisoning: trends in blood lead levels in unchelated children. *Environ Health Perspect.* 1996;104(9):968-972.
158. Office of Policy Development and Research Department of Housing and Urban Development. Lead-based paint abatement demonstration (FHA). *Washington, DC: Department of Housing and Urban Development.* 1991;(Publication no. HUD-1316-PDR).
159. Farfel MR, Chisolm JJ, Jr., Rohde CA. The longer-term effectiveness of residential lead paint abatement. *Environ Res.* 1994;66(2):217-221.
160. Clark S, Grote J, Wilson J, et al. Occurrence and determinants of increases in blood lead levels in children shortly after lead hazard control activities. *Environ Res.* 2004;96(2):196-205.

161. Rhoads G, Ettinger A, Weisel C, al. e. The effect of dust lead control on blood lead in toddlers: a randomized trial. *Pediatrics.* 1999;103(3):551-555.
162. Taha T, Kanarek MS, Schultz BD, Murphy A. Low-cost household paint abatement to reduce children's blood lead levels. *Environ Res.* 1999;81(4):334-338.
163. Aschengrau A, Hardy S, Mackey P, Pultinas D. The impact of low technology lead hazard reduction activities among children with mildly elevated blood lead levels. *Environ Res.* 1998;79(1):41-50.
164. Leighton J, Klitzman S, Sedlar S, Matte T, Cohen NL. The effect of lead-based paint hazard remediation on blood lead levels of lead poisoned children in New York City. *Environ Res.* 2003;92(3):182-190.
165. Haynes E, Lanphear BP, Tohn E, Farr N, Rhoads GG. The effect of interior lead hazard controls on children's blood lead concentrations: a systematic evaluation. *Environ Health Perspect.* 2002;110(1):103-107.
166. Yiin LM, Lioy PJ, Rhoads GG. Impact of home carpets on childhood lead intervention study. *Environ Res.* 2003;92(2):161-165.
167. Campbell C, Schwarz DF, Rich D, Dockery DW. Effect of a follow-up professional home cleaning on serial dust and blood lead levels of urban children. *Arch Environ Health.* 2003;58(12):771-780.
168. Swindell SL, Charney E, Brown MJ, Delaney J. Home abatement and blood lead changes in children with class III lead poisoning. *Clin Pediatr.* 1994;33(9):536-541.
169. Brown MJ, Gardner J, Sargent JD, Swartz K, Hu H, Timperi R. The effectiveness of housing policies in reducing children's lead exposure. *Am J Public Health.* 2001;91(4):621-624.
170. Galke W, Clark S, Wilson J, et al. Evaluation of the HUD lead hazard control grant program: early overall findings. *Environ Res.* 2001;86(2):149-156.
171. Strauss W, Pivetz T, Ashley P, Menkedick J, Slone E, Cameron S. Evaluation of lead hazard control treatments in four Massachusetts communities through analysis of blood-lead surveillance data. *Environ Res* 2005;in press.
172. Foster JD, Louria DB, Stinson L. Influence of documented lead poisoning on environmental modification programs in Newark, New Jersey. *Arch Environ Health.* 1979;34(5):368-371.
173. Weitzman M, Aschengrau A, Bellinger D, Jones R, Hamlin JS, Beiser A. Lead-contaminated soil abatement and urban children's blood lead levels. *JAMA.* 1993;269(13):1647-1654.
174. Environmental Protection Agency. Three city urban soil lead abatement demonstration project (fact sheet). *Washington, DC: Environmental Protection Agency.* 1992;(Publication no. 9355.4-10FSa).
175. Farrell KP, Brophy MC, Chisolm JJ, Jr., Rohde CA, Strauss WJ. Soil lead abatement and children's blood lead levels in an urban setting. *Am J Public Health.* 1998;88(12):1837-1839.
176. Charney E, Kessler B, Farfel M, Jackson D. Childhood lead poisoning. A controlled trial of the effect of dust-control measures on blood lead levels. *N Engl J Med.* 1983;309(18):1089-1093.
177. Jordan CM, Yust BL, Robison LL, Hannan P, Deinard AS. A randomized trial of education to prevent lead burden in children at high risk for lead exposure: efficacy as measured by blood lead monitoring. *Environ Health Perspect.* 2003;111(16):1947-1951.

178. Lanphear BP, Howard C, Eberly S, et al. Primary prevention of childhood lead exposure: A randomized trial of dust control. *Pediatrics.* 1999;103(4 Pt 1):772-777.
179. Schultz B, Pawel D, Murphy A. A retrospective examination of in-home educational visits to reduce childhood lead levels. *Environ Res.* 1999;80(4):364-368.
180. Kimbrough R, LeVois M, Webb D. Survey of lead exposure around a closed lead smelter. *Pediatrics.* 1995;95(4):550-554.
181. Porru S, Donato F, Apostoli P, Coniglio L, Duca P, Alessio L. The utility of health education among lead workers: the experience of one program. *Am J Ind Med.* 1993;23(3):473-481.
182. Aschengrau A, Beiser A, Bellinger D, Copenhafer D, Weitzman M. The impact of soil lead abatement on urban children's blood lead levels: phase II results from the Boston Lead-In-Soil Demonstration Project. *Environ Res.* 1994;67(2):125-148.
183. Aschengrau A, Beiser A, Bellinger D, Copenhafer D, Weitzman M. Residential lead-based-paint hazard remediation and soil lead abatement: their impact among children with mildly elevated blood lead levels. *Am J Public Health.* 1997;87(10):1698-1702.
184. Lanphear BP, Succop P, Roda S, Henningsen G. The effect of soil abatement on blood lead levels in children living near a former smelting and milling operation. *Public Health Rep.* 2003;118(2):83-91.
185. Dalton MA, Sargent JD, O'Connor GT, Olmstead EM, Klein RZ. Calcium and phosphorus supplementation of iron-fortified infant formula: no effect on iron status of healthy full-term infants. *Am J Clin Nutr.* 1997;65(4):921-926.
186. Gallicchio L, Scherer RW, Sexton M. Influence of nutrient intake on blood lead levels of young children at risk for lead poisoning. *Environ Health Perspect.* 2002;110(12).
187. Hammad TA, Sexton M, Langenberg P. Relationship between blood lead and dietary iron intake in preschool children. A cross-sectional study. *Ann Epidemiol.* 1996;6(1):30-33.
188. Lucas SR, Sexton M, Langenberg P. Relationship between blood lead and nutritional factors in preschool children: a cross-sectional study. *Pediatrics.* 1996;97(1):74-78.
189. Markowitz ME, Sinnett M, Rosen JF. A randomized trial of calcium supplementation for childhood lead poisoning. *Pediatrics.* 2004;113(1 Pt 1).
190. Sargent JD, Dalton MA, O'Connor GT, Olmstead EM, Klein RZ. Randomized trial of calcium glycerophosphate-supplemented infant formula to prevent lead absorption. *Am J Clin Nutr.* 1999;69(6):1224-1230.
191. Schell LM, Denham M, Stark AD, Ravenscroft J, Parsons P, Schulte E. Relationship between blood lead concentration and dietary intakes of infants from 3 to 12 months of age. *Environ Res.* 2004;96(3):264-273.
192. Schell LM, Denham M, Stark AD, et al. Maternal blood lead concentration, diet during pregnancy, and anthropometry predict neonatal blood lead in a socioeconomically disadvantaged population. *Environ Health Perspect.* 2003;111(2):195-200.
193. Simon JA, Hudes ES. Relationship of ascorbic acid to blood lead levels. *JAMA.* 1999;281(24):2289-2293.
194. Zierold KM, Anderson H. Trends in blood lead levels among children enrolled in the Special Supplemental Nutrition Program for Women, Infants, and Children from 1996 to 2000. *Am J Public Health.* 2004;94(9):1513-1515.
195. Lanphear BP, Hornung R, Ho M, Howard CR, Eberly S, Knauf K. Environmental lead exposure during early childhood. *J Pediatr.* 2002;140(1):40-47.

196. Haynes E, Kalkwarf H, Hornung R, al. e. Vitamin D Fok1 polymorphism and blood lead concentration in children. *Environ Health Perspect.* 2003;111:1665-1669.
197. Bellinger D. Teratogen Update: Lead and Pregnancy. *Birth Defects Research.* 2004;(Part A) 73:409-420.
198. Glotzer DE, Bauchner H. Management of childhood lead poisoning: a survey. *Pediatrics.* 1992;89:614-618.
199. Markowitz ME, Rosen JF. Need for the lead mobilization test in children with lead poisoning. *J Pediatr.* 1991;119(2):305-310.
200. Farfel MR, Chisolm JJ, Jr. Health and environmental outcomes of traditional and modified practices for abatement of residential lead-based paint. *Am J Public Health.* 1990;80(10):1240-1245.
201. Amitai Y, Brown MJ, Graef JW, Cosgrove E. Residential deleading: effects on the blood lead levels of lead-poisoned children. *Pediatrics.* 1991;88(5):893-897.
202. Amitai Y, Graef JW, Brown MJ, Gerstle RS, Kahn N, Cochrane PE. Hazards of 'deleading' homes of children with lead poisoning. *Am J Dis Child.* 1987;141(7):758-760.
203. Rey-Alvarez S, Menke-Hargrave T. Deleading dilemma: pitfall in the management of childhood lead poisoning. *Pediatrics.* 1987;79(2):214-217.
204. Feldman RG. Urban lead mining: lead intoxication among deleaders. *N Engl J Med.* 1978;298(20):1143-1145.
205. Chisolm JJ, Jr. Treatment of acute lead intoxication--choice of chelating agents and supportive therapeutic measures. *Clin Toxicol.* 1970;3(4):527-540.
206. Moel DI, Kumar K. Reversible nephrotoxic reactions to a combined 2,3-dimercapto-1-propanol and calcium disodium ethylenediaminetetraacetic acid regimen in asymptomatic children with elevated blood lead levels. *Pediatrics.* 1982;70(2):259-262.
207. Shannon MW, Townsend MK. Adverse effects of reduced-dose d-penicillamine in children with mild-to-moderate lead poisoning. *Ann Pharmacother.* 2000;34(1):15-18.
208. Mann KV, Travers JD. Succimer, an oral lead chelator. *Clin Pharm.* 1991;10(12):914-922.
209. Lane WG, Kemper AR, American College of Preventive M. American College of Preventive Medicine Practice Policy Statement. Screening for elevated blood lead levels in children. *Am J Prev Med.* 2001;20(1):78-82.
210. American Academy of Pediatrics Committee on Environmental Health. Screening for elevated blood lead levels. *Pediatrics.* 1998;101(6):1072-1078.
211. Ellis MR, Kane KY. Lightening the lead load in children. *Am Fam Physician.* 2000;62(3):545-554.
212. Centers for Medicare and Medicaid Services. Medicaid and EPSDT. Added 6.8.05; http://www.cms.hhs.gov/medicaid/epsdt/default.asp. Accessed June 5, 2005.
213. Markowitz M, Rosen JF, Clemente I. Clinician follow-up of children screened for lead poisoning. *Am J Public Health.* 1999;89(7):1088-1090.
214. Campbell JR, Schaffer SJ, Szilagyi PG, O'Connor KG, Briss P, Weitzman M. Blood lead screening practices among US pediatricians. *Pediatrics.* 1996;98(3 Pt 1):372-377.
215. New York State Department of Health and American College of Obstetricians and Gynecologists District II. *Lead poisoning prevention guidelines for prenatal care providers.* Albany, NY: New York City Department of Health; 1995.

216. Pirkle JL, Brody DJ, Gunter EW, et al. The decline in blood lead levels in the United States. The National Health and Nutrition Examination Surveys (NHANES) *JAMA.* 1994;272(4):284-291.
217. Annest JL, Pirkle JL, Makuc D, Neese JW, Bayse DD, Kovar MG. Chronological trend in blood lead levels between 1976 and 1980. *N Engl J Med.* 1983;308(23):1373-1377.
218. Centers for Disease Control and Prevention. Blood lead levels - United States, 1988-1991. *MMWR.* 1994;43:545-548.
219. Hayes EB, McElvaine MD, Orbach HG, Fernandez AM, Lyne S, Matte TD. Long-term trends in blood lead levels among children in Chicago: relationship to air lead levels. *Pediatrics.* 1994;93(2):195-200.
220. Davis JM, Elias RW, Grant LD. Current issues in human lead exposure and regulation of lead. *Neurotoxicology.* 1993;14(2-3):15-27.
221. Galal-Gorchev H. Dietary intake, levels in food and estimated intake of lead, cadmium, and mercury. *Food Addit Contam.* 1993;10(1):115-128.
222. Prpic-Majic D, Pongracic J, Hrsak J, Pizent A. A follow-up study in a lead smelter community following the introduction of an effective pollution control system. *Isr J Med Sci.* 1992;28(8-9):548-556.
223. Yankel AJ, von Lindern IH, Walter SD. The Silver Valley lead study: the relationship between childhood blood lead levels and environmental exposure. *J Air Pollut Control Assoc.* 1977;27(8):763-767.
224. Department of Health and Human Services, Department of Housing and Urban Development, and Environmental Protection Agency. Report of the Interagency Task Force on the Prevention of Lead Poisoning: a report to Congress. *Washington, DC: Department of Housing and Urban Development.* 1993.